Immediate and short-term effect of balloonmitral valvuloplasty on circumferential strain, global and regional biventricular systolic function: a two-dimensionalstrain echocardiographic study

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Abstract: Background: Two-dimensional strain has been developed for the quantitative assessment of global and regional myocardial function. Two-dimensional strain represents a novel technique to predict subclinical ventricular dysfunction in many diseases as ischemic heart disease with preserved ventricular function and hypertrophic cardiomyopathy. We use this technique in assessing regional, global longitudinal strain of both LV and RV and circumferential strain of LV before and after BMV done for patients with Rheumatic MS. **Introduction**: Mitral stenosis (MS) is the most common valve lesion in chronic RHD. Several mechanisms have been postulated to explain left ventricle (LV) systolic dysfunction in patients with MS, including chronically reduced preload, resulting in adverse LV remodeling, and the extension of inflammatory process from the mitral valve apparatus into the adjacent myocardium. Systolic dysfunction of the right ventricle (RV) is well documented in patients with rheumatic MS; RV dysfunction is usually overlooked before the emergence of clinical signs of systemic venous congestion because of difficulties in the quantitative of RV function. **Aim of the study:** Assessment of the immediate and short term effect of balloon mitral valvuloplasty (BMV) on circumferential strain, global and regional biventricular systolic function using 2D TTE strain. **Methods and results:** Twenty patients with mitral stenosis (MS) and 20 healthy subjects underwent full echocardiographic examinations, including left ventricle (LV) and right ventricle (RV) regional and global longitudinal strain (GLS) measurements. In MS patients, measurements were repeated within 24 h and 1 month after BMV. Patients with MS had lower LV and RV GLS compared with control (15.15±1.76 vs 20.95±1.43, P<0.001) and (17.55±2.45 vs -19.35±2.54 VS, P=0.031), respectively, at baseline before BMV. Significant decrease was noted in the basal and septal segments compared with the apical LV segments and basal RV free wall. BMV resulted in significant improvement in LV and RV GLS within 24 h post-BMV compared with baseline values (P < 0. 001 and <0.001, respectively), an improvement which was maintained after month. There was significant positive correlation between both LV and RV GLS at baseline and mitral valve mean pressure gradient and RV systolic pressure and significant inverse correlation between LV GLS and MVA. **Conclusion:** MS patients have subclinical LV and RV systolic dysfunction by GLS despite normal ejection fraction and fractional area change. BMV results in marked improvement in LV and RV GLS as well as CS immediately post-BMV with trend towards normalization at follow-up after 1 month. A mixed etiology theory involving a myocardial as well as a hemodynamic factor is believed to be the cause for this subclinical biventricular dysfunction and its improvement at short-term follow-up post-BMV. **Recommendations:** The presence of subclinical affection of LV function in patients with MS and the significant sustained improvement in GLS of LV & RV also CS during short-term follow-up post-BMV proved in this study should have their impact on the current guidelines for BMV, so that we may consider in the future BMV for patients with impaired LV GLS in order to protect these patients from developing progressive LV systolic dysfunction. In addition, we recommend further study of the CS of LV in order to detect subclinical affection in patients with MS.

Keywords: Two-dimensional strain - Global longitudinal strain – Circumferential strain –balloon mitral valvuloplasty - mitral valve area – Rheumatic heart disease - mitral stenosis.

1. Introduction

Rheumatic heart disease (RHD) is one of the most common forms of cardiac diseases, particularly in developing countries, where it remains the second most common cause of cardiovascular morbidity and mortality after atherosclerotic vascular disease[1 – 3]. Mitral stenosis (MS) is the most common valve lesion in chronic RHD. Several mechanisms have been postulated to explain left ventricle (LV) systolic dysfunction in patients with MS, including chronically reduced preload, resulting in adverse LV remodeling, and the extension of inflammatory process from the mitral valve apparatus into the adjacent myocardium[4]. Systolic dysfunction of the right ventricle (RV) is well

documented in patients with rheumatic MS; RV dysfunction is usually overlooked before the emergence of clinical signs of systemic venous congestion because of difficulties in the quantitative of RV function[5 − 7]. Nowadays, a novel method, 2D strain, has been developed for the quantitative assessment of global and regional myocardial function[8,9]. Two-dimensional strain represents a novel technique to predict subclinical ventricular dysfunction in many diseases as ischemic heart disease with preserved ventricular function[10] and hypertrophic cardiomyopathy[11]. The use of such technique to predict subclinical affection of biventricular function in MS patients and effect of BMV on this affection is lacking. The objective of this study was to assess global and regional LV and RV functions and CS using 2D strain in patients with MS before and after BMV. We postulate that the subtle changes in RV and LV functions in these patients will be evident using global longitudinal strain (GLS) despite presence of normal ventricular functions and that BMV will have its positive effect on these subtle changes.

2. Patients and methods
Patient population
This was a prospective observational study which included patients underwent elective BMV in the Cardiology Department of Bab El She'ryia University Hospital in the period from October 2015 to September 2016. The study included 20 patients and 20 healthy age- and sex-matched controls. The inclusion criteria for the study group were as follows: (i) patients' age from 21 to 45 years. (ii) Symptomatic moderate-to-severe MS. (iii) Asymptomatic moderate-to-severe MS with significant pulmonary hypertension (ESPAP more than 50 mmHg at rest). The exclusion criteria were as follows: (i) patients with mild MS (MVA more than 1.5 cm). (ii) Patients who are not candidates for BMV (due to either Wilkins score ≥10, commissural calcification or left atrial thrombus). (iii)Moderate-to-severe valvular disease other than MS. (iv) Congenital MS. (v) Patients with organic tricuspid valve disease. (vi) Evidence of rheumatic activity during the preceding 6 months.(vii) Patients with impaired LV systolic function (defined as EF, 54% using modified Simpson's rule)[12]. (viii) Patients with clinical evidence of right-sided heart failure. (ix) Patients with atrial fibrillation or other atrial arrhythmias. (x) Patients with atrioventricular conduction abnormalities. (xi) Patients with hypertension, diabetes, or ischemic heart disease. (xii) Patients with chronic obstructive pulmonary disease. (xiii) Patients with pulmonary thromboembolic disease.
Echocardiographic and clinical data collection

All patients were subjected to the following: Informed verbal consent, full history taking. All patients were assessed clinically with full cardiological examination & resting 12 leads ECG was done to all. All patients (including control group) were studied in the left lateral decubitus position using an ultrasound system (Model Philips IE 33, Philips Medical Systems, USA)) using X5 & S5 transducers 3.5 MHZ**.** Standard 2D and M-mode echocardiograms were obtained. Basic measurements included LV wall thickness, LV internal dimensions, LV end-diastolic, and end-systolic volumes, LV EF by M mode and modified Simpson's rule, left atrial (LA) anterior – posterior dimensions, left atrial end-diastolic volume, RV end-diastolic(RVEDA) and end-systolic areas(RVESA), RV fractional area change (RVFAC) which is calculated as(RVEDA - RVESA)/RVEDA X 100 and tricuspid annular plane systolic excursion13The conventional indices for assessment of the severity of MS; MVA by planimetry and pressure half-time and the mean mitral valve pressure gradients and PASP were measured as recommened[14].
2D strain imaging
2D echocardiography images were obtained from para sternal short axis at the level of MV to get circumferential strain (global & segmental) LV apical long axis apical three chamber, apical four- and two-chamber views and modified apical view for RV. All images were obtained during breath hold, and stored in cine-loop format from three ormore consecutive beats. The frame rate for images was between 50 and 90 frames/s. All data were saved for further offline analysis. After defining the endocardial border manually and adjusting the ROI width, an epicardial tracing was automatically developed by the software system in the following sequence: para sternal short axis (MV level) for a circumferential strain (global & segmental) apical long axis, apical four-chamber, and apical two-chamber for LV and modified apical view for RV. For each view, the endocardial border was manually traced in the end-systolic frame. The software then automatically generated myocardial strain curves by frame-by-frame tracking of the natural acoustic markers throughout the cardiac cycle. If the automatically obtained tracking segments were adequate for analysis, the software system was allowed to read the data, whereas analytically inadequate tracking segments were either corrected manually or excluded from the analysis. The myocardium of the LV in apical views was automatically divided into six walls (anterior septum, inferolateral, anterior, inferior, inferior septum & lateral,)and the myocardium of RV was divided into two walls (septum and RV free wall), all walls were then subdivided into three segments (apical, mid, and basal)while the myocardium of the LV in para sternal

view short axis MV level was devided into sex segments (anterior, anteroseptum, anterolateral, inferior, inferolateral & inferoseptum). In blinded post-processing, longitudinal and circumferential deformation had been assessed by speckle tracking, being measured the peak systolic longitudinal strain (SPLS) for the 17 segment LV model from the apical 4-chambers, 2-chambers and long axis views, with high frame rates (> 60 frames/s) using Q LAB. End-systole was defined as aortic valve closure in the apical long-axis view by continuous Doppler wave recording. Automated delineation of endocardial borders was obtained through marking the mitral annulus level and at the apex on each digital loop. The area of interest was manually adjusted if automated delineation was not optimal. Segments with poor image acquisition or artifacts were excluded due to inability to measure LS. Segmental LS was calculated as the percentage of lengthening or shortening and the results for each plane were displayed. The peak systolic circumferential strain (SPCS) for 6 segments protocol were calculated from the short axis views at the level of mitral valve with high frame rates (> 60 frames/s).

Follow-up echocardiogram

All patients in the study group underwent full echocardiographic study including 2D strain of both RV and LV and CS within24 h and after 1 month post-BMV using the same machine for transthoracic echocardiogram (Follow-up study).

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 23.0 for windows. Data are presented as the Mean ± standard deviation (SD), frequency, and percentage. Categorical variables were compared using the chi-square ($\chi 2$) and Fisher's exact tests (if required). Continuous variables were compared by the Student t test (two-tailed) for parametric data. Mann-Whitney U test was used to compare continuous nonparametric data. Paired sample T test was used to compare two 2 related samples for normally distributed data and Wilcoxon signed – rank and Friedman's ANOVA tests were used to compare related samples of data which were abnormally distributed. The level of significance was accepted if the P value < 0.05.

3. Results

Out of 50 patients referred to our hospital in the specified period of time for elective BMV, 20 patients were enrolled in this study. Ten patients were not fit for BMV due to presence of LA thrombus by trans-esophageal echocardiographic study. The remaining 20 patients underwent BMV but were excluded from the study due to presence of comorbidities that might

affect the LV-GLS values e.g. diabetes, hypertension and atrial fibrillation. Of the excluded patients 3 had concomitant LV dysfunction defined as EF≤54%.

Table (1): Demographic data of the studied sample.

Variables	No. (N= 40)	%
Group Patient	20	50.0
Control	20	50.0
Gender Male	13	32.5
Female	27	67.5
Age (M ± SD)	28.93 ± 6.07	

Table (2): Comparison baseline echocardiographic parameters between patients pre BMV and control groups.

Parameters		M ± SD			P
LAD	Patient	5.09	±	0.74	< **0.001**
	Control	35.46	±	2.30	
LVEDD	Patient	47.3	±	0.61	0.23
	Control	47.01	±	0.99	
LVESD	Patient	31.3	±	0.55	0.75
	Control	30.24	±	2.89	
EF SIM	Patient	57.70	±	2.39	0.931
	Control	57.59	±	5.38	
LVEDV	Patient	85.80	±	16.65	< **0.001**
	Control	108.95	±	17.85	
LVESV	Patient	36.95	±	7.39	**0.001**
	Control	46.90	±	10.03	
LAV	Patient	104.15	±	29.06	< **0.001**
	Control	37.35	±	8.38	
RVESV	Patient	18.35	±	2.92	0.054
	Control	20.45	±	3.72	
RVEDV	Patient	34.40	±	4.17	**0.021**
	Control	37.20	±	3.11	
FAC	Patient	44.16	±	3.32	0.41
	Control	45.03	±	6.90	

Table (3): Comparison of speckle tracking echocardiographic, global longitudinal strain, between patients and control groups.

Parameters		M	±	SD	P
AP2	Patients	-13.75	±	1.65	< **0.001**
	Control	-20.55	±	1.76	
AP4C	Patients	-15.05	±	2.19	< **0.001**
	Control	-21.35	±	1.93	
LAX(3C)	Patients	-14.70	±	2.77	< **0.001**
	Control	-20.50	±	1.73	
GLS LV	Patients	-15.15	±	1.76	< **0.001**
	Control	-20.95	±	1.43	

Table (4): Comparison of LV segmental speckle tracking echocardiographic parameters between patients pre BMV and control groups.

Parameters		M	±	SD	P
A ANT	Patients	-9.35	±	1.84	< 0.001
	Control	-19.45	±	2.39	
AP INF	Patients	-20.30	±	4.26	0.263
	Control	-21.60	±	2.84	
AP IL	Patients	-14.50	±	3.33	< 0.001
	Control	-21.30	±	3.28	
AP LAT	Patients	-13.10	±	2.10	< 0.001
	Control	-18.80	±	5.97	
AP AS	Patients	-16.25	±	9.26	0.051
	Control	-20.60	±	2.72	
AP IS	Patients	-21.05	±	3.10	0.747
	Control	-21.35	±	2.72	
B ANT	Patients	-14.37	±	3.04	< 0.001
	Control	-21.30	±	3.13	
B AS	Patients	-10.85	±	1.31	< 0.001
	Control	-21.35	±	2.78	
B IS	Patients	-9.80	±	8.53	< 0.001
	Control	-20.55	±	3.30	
B INF	Patients	-19.55	±	2.96	< 0.001
	Control	-22.95	±	2.35	
B LAT	Patients	-20.45	±	2.42	0.006
	Control	-22.90	±	2.90	
B IL	Patients	-15.95	±	2.54	< 0.001
	Control	-21.35	±	2.89	
M ANT	Patients	-16.35	±	3.83	< 0.001
	Control	-21.10	±	2.69	
M AS	Patients	-18.90	±	1.33	0.027
	Control	-20.45	±	2.70	
M IS	Patients	-14.95	±	1.19	< 0.001
	Control	-22.40	±	2.52	
M INF	Patients	-19.40	±	1.14	0.001
	Control	-22.30	±	3.29	
M IL	Patients	-16.55	±	3.19	< 0.001
	Control	-21.20	±	2.89	
M LAT	Patients	-17.40	±	1.19	< 0.001
	Control	-21.25	±	2.88	

Table (5): Comparison of speckle tracking echocardiographic, circumferential strain, between patients pre BMV and control groups.

Parameters		M	±	SD	P
CS	Patients	-17.05	±	2.70	< 0.001
	Control	-27.65	±	5.67	

Table (6): Comparison of speckle tracking echocardiographic, right ventricular strain, between patients and control groups.

Parameters		M	±	SD	P
B RV S	Patients	-10.05	±	1.32	<
	Control	-18.00	±	1.26	0.001
M RV S	Patients	-11.75	±	2.22	<
	Control	-18.20	±	1.15	0.001
AP RV S	Patients	-20.70	±	2.77	<
	Control	-17.75	±	1.48	0.001
B RV FW	Patients	-16.40	±	3.53	<
	Control	-22.25	±	2.10	0.001
M RVF W	Patients	-24.35	±	3.59	0.003
	Control	-21.50	±	1.85	
AP FW	Patients	-23.60	±	3.23	0.001
	Control	-20.50	±	2.21	
G RV	Patients	-17.55	±	2.54	0.031
	Control	-19.35	±	2.54	

Table (7) and figure (1): Comparison of MVA and MPG pre-& post BMV.

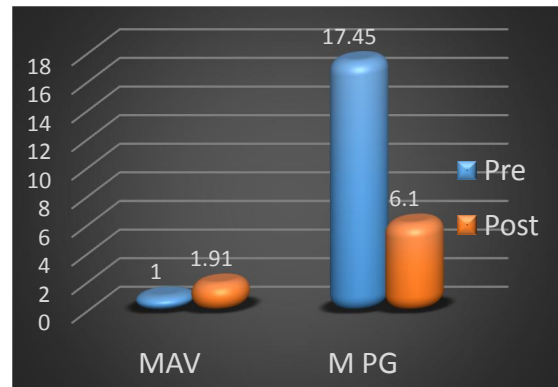| Parameters		M	±	SD	P
MAV (2D)	Pre	1.0	±	0.15	< 0.001
	Post	1.91	±	0.22	
M PG	Pre	17.45	±	6.68	< 0.001
	Post	6.10	±	2.25	

Table (8): Comparison between baseline echocardiographic parameters measured in the study group before BMV and 24 hours post.

Parameters		M ± SD			P
LAD	Pre	5.09	±	0.74	<
	Post	4.52	±	0.45	**0.001**
LVEDD	Pre	4.73	±	0.61	<
	Post	5.03	±	0.54	**0.001**
LVESD	Pre	3.13	±	0.55	**0.033**
	Post	3.29	±	0.52	
EF SIM	Pre	57.70	±	2.39	<
	Post	60.50	±	2.69	**0.001**
LVEDV	Pre	85.80	±	16.65	<
	Post	99.10	±	21.82	**0.001**
LVESV	Pre	36.95	±	7.39	<
	Post	42.65	±	7.92	**0.001**
LAV D	Pre	104.15	±	29.06	<
	Post	80.50	±	25.71	**0.001**
RVESV	Pre	18.35	±	2.92	<
	Post	11.70	±	2.03	**0.001**
RVEDV	Pre	34.40	±	4.17	<
	Post	24.60	±	4.01	**0.001**
FAC	Pre	46.16	±	3.32	<
	Post	50.77	±	4.41	**0.001**

Table (9) and figure (2): Comparison between RV systolic pressure measured in the study group before and immediately & 1 month after BMV.

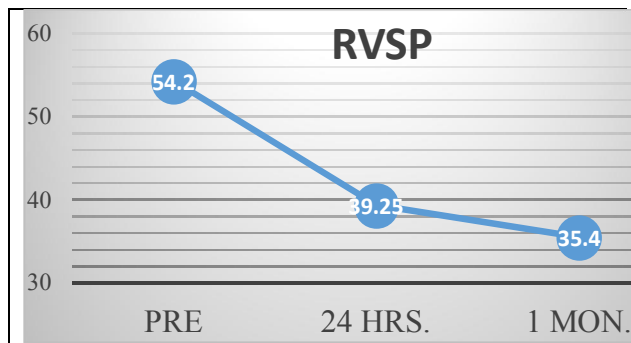| Parameters		M	±	SD	P
	Pre	54.20	±	14.55	
RVSP	24 hrs. post.	39.25	±	9.30	**< 0.001**
	1 mon. post.	35.40	±	8.61	

Table (10) and figure (3): Comparison between LV global strain (longitudinal & circumferential) and RV global strain measured in the study group before BMV, 24 HS post& 1 month after BMV.

| Parameters		M	±	SD	p
AP2	Pre	-13.75	±	1.65	<
	24 hrs. post.	-18.25	±	2.02	**0.001**
	1 mon. post.	-21.65	±	2.39	
AP4C	Pre	-15.05	±	2.19	<
	24 hrs. post.	-19.60	±	1.96	**0.001**
	1 mon. post.	-21.75	±	2.07	
LAX (3C)	Pre	-14.70	±	2.77	<
	24 hrs. post.	-18.50	±	2.46	**0.001**
	1 mon. post.	-20.55	±	2.44	
GLS LV	Pre	-15.15	±	1.76	<
	24 hrs. post.	-18.70	±	1.72	**0.001**
	1 mon. post.	-20.75	±	1.92	
CS	Pre	-17.05	±	2.70	<
	24 hrs. post.	-21.90	±	2.83	**0.001**
	1 mon. post.	-23.75	±	2.20	
G RV	Pre	-17.55	±	2.54	<
	24 hrs. post.	-23.40	±	2.62	**0.001**
	1 mon. post.	-26.65	±	2.92	
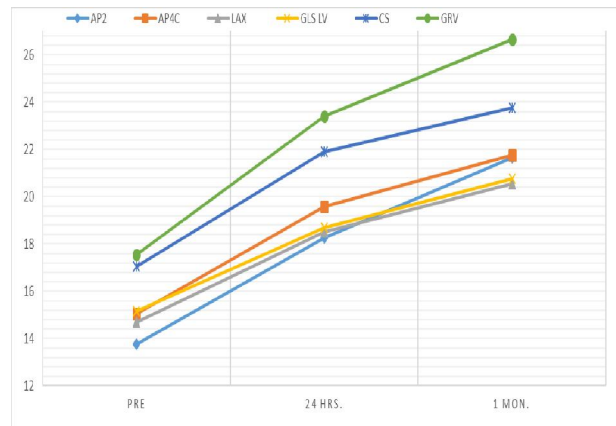
Figure (3): Comparison between LV global strain (longitudinal & circumferential) and RV global strain measured in the study group before immediately & 1 month after BMV
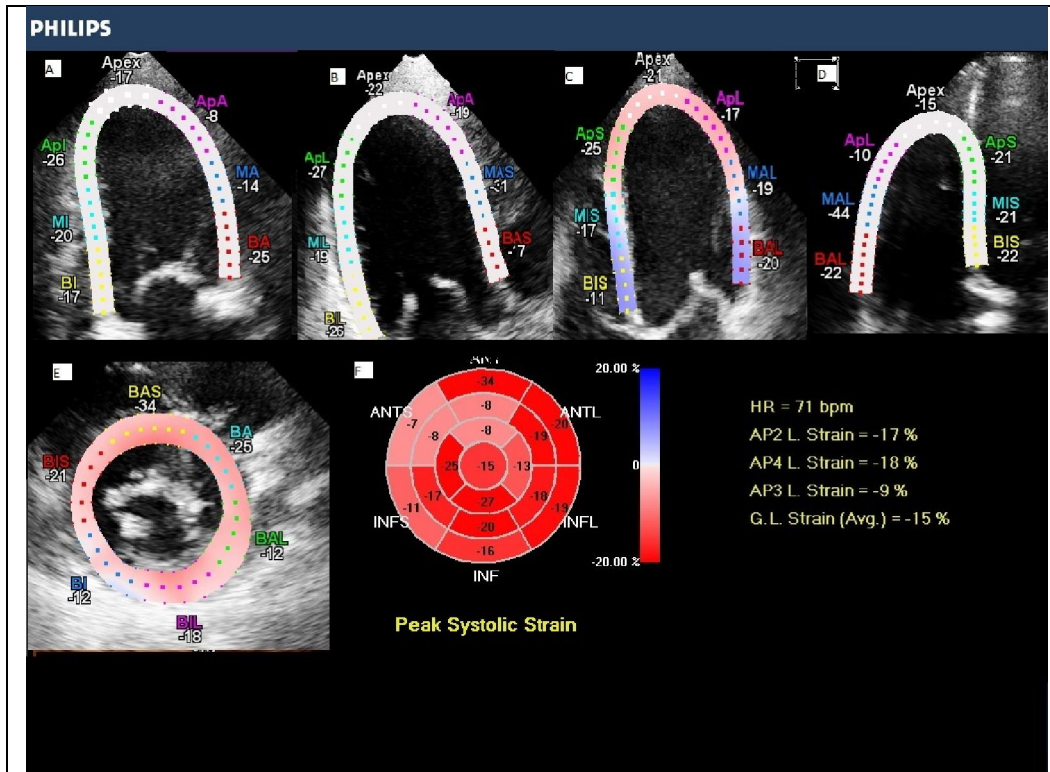
Figure (4): 2D strain analysis of the LV as traced in the apical four-chamber pre (left side) and post BMV (right side).
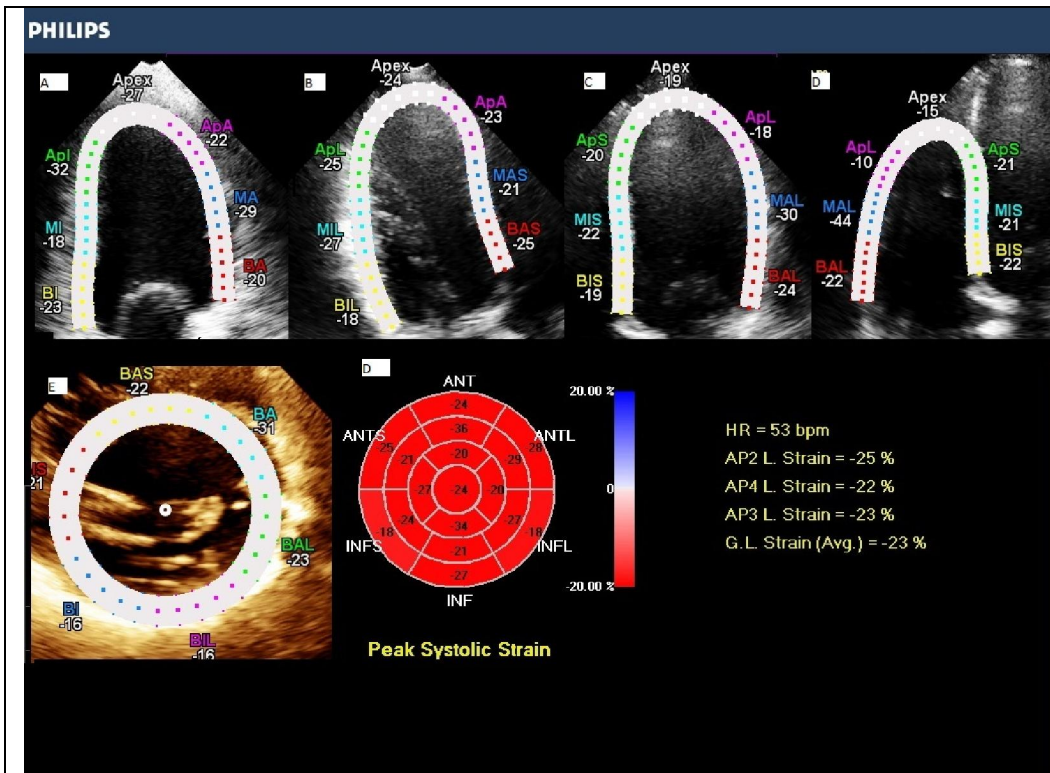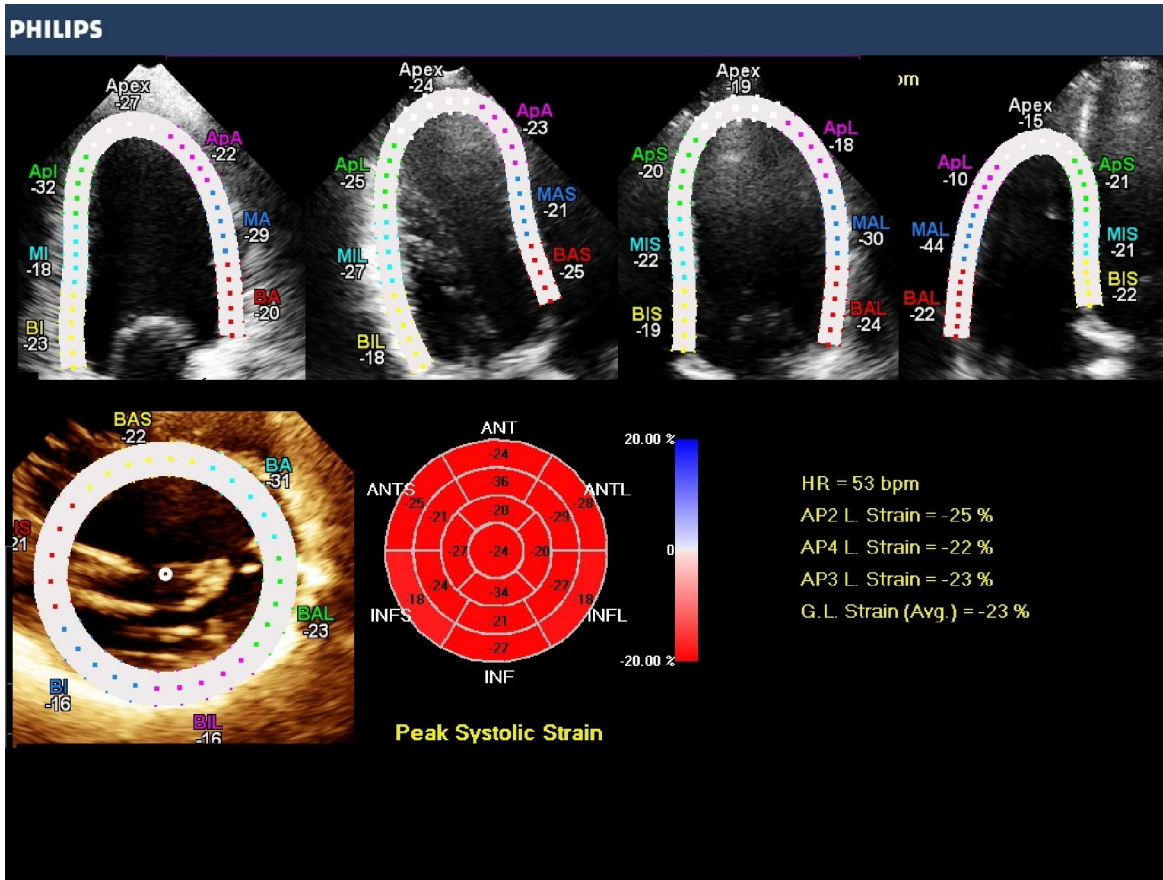

Figure (5): 2D Longitudinal strain of the RV pre (left side) and post BMV (right side)in the same patient.

Figure (6): Comparison between LV global strain (longitudinal & circumferential) and RV global strain measured in the study group before immediately & 1 month after BMV.

4. Discussion

Although there is a downwards trend in the prevalence of MS in developed countries, it stands out as a huge public health problem in developing countries. Few studies have reported that LV systolic dysfunction may not be uncommon and may indeed contribute to the development of symptoms in patients with MS[15]. The researches for the most appropriate method to measure contractile characteristics of myocardium are still carrying on[22]. Nowadays, a novel method, 2D strain, has been developed for the quantitative assessment of global and regional myocardial function[23]. This study did not study the effect of MS on global and regional subclinical biventricular function only, but also systematically evaluated the effect of BMV on these functions using GLS & CS immediately and after 1month post-BMV. As regard the study, the mean age of patients with MS was (28.93 ± 6.07). The mean duration of symptoms was 3.1± 4.2 years; all patients were in NYHA class II – III. Baseline echocardiographic parameters are shown in table (2). There was no significant difference between the study group and the control group as regard LV dimensions, LV function by modified

Simpsons' method, and RV function by FAC. There was significant difference between the study group and the control group as regard LA antero-posterior diameter (5.09±0.74 vs 35.46±2.30, p<0.001) & LA volume (104.15±29.06 vs37.35±8.3, p<0.001), which is be due to increase LA pressure due to valve stenosis & LV volumes (LVEDV & LVESV), 85.8± 16.65 vs 108.95±17.85, p<.001 and 36.95±7.39 vs 46.9±10.03, P<.001 respectively). that is may be due to decrease flow across the mitral valve and decrease LV filling. Most of the patients in the study group underwent successful BMV with significant increase in planimetry measured MVA (1.0±0.15 vs 1.91±0.22, p<0.001) as well as significant drop in mean PG across the mitral valve (17.45±6.68 vs 6.1±2.25, p<0.001) and pulmonary artery systolic pressure (54.2±14.55 VS 39.35±9.3, p<0.001) (Table 7). There was significant decrease in LA diastolic dimension with base line measurements before BMV (5.09±0.74 VS 4.52±0.45, P<0.001 and diastolic volume (104.15±29.06 vs 80.5±25.71, p<0.001). There was also significant increase in LV end -diastolic and systolic volumes (85.8±16.65 VS 99.1±21.82, P<0.001 and 36.95±7.39 VS 42.65±7.92, P<0.001)

respectively. There is also significant increase in EF (57.7±2.93 VS 60.50±2.69, P<0.001). There was significant decrease in RV volumes (RVESV &RVEDV) (18.35±2.92 vs 11.7±2.03, p<0.001 and 34.4±4.17 vs 24.6±4.01, p<0.001) respectively immediately after BMV. There was significant increase in RV FAC (46.16±3.32 VS 50.77±4.41, P<0.001). The decrease in LA dimension and volume may be due to decrease pressure across the mitral valve after balloon dilatation of the MS. While the increase in LV dimension systolic & diastolic and accordingly EF is due to increase flow through the MV after dilatation (increase LV filling) **(hemodynamic effect).** As regard RV volumes & FAC; the decrease in volumes may be due to decrease LA pressure and accordingly decrease PVR &also may be due to decrease RVSP. Compared with the control group, patients had significantly lower LV and RV GLS (-15.15±1.76 vs 20.95±1.43, P<0.001) and (-17.55±2.45 vs -19.35±2.54 VS, P=0.031), respectively, at baseline before BMV (Table 3). Although, compared with the control group, patients had significantly lower circumferential strain (CS) (MV level) (-17.05±1.43 vs -27.65±5.67, P=0.001) (table 5). The significant decrease in the LV GLS values compared with control group was significant throughout the whole segments with the exception of the apical inferior, apical antero-septum and apical inferior septum (Tables (4). On the other hand, the decrease in RV GLS vs. control group was only significant in the septalsegments (mid& basal) only and basal RV free wall (Table 6). While there is increase in segmental LS of the RV vs control group was noticed in other segments (apical RV septum, mid RV free wall and apical RV free wall), but the net of the total segments was decrease in RV GLS in the study group compared to control group (Table 6). Immediately after BMV, there was significant improvement in LV GLS in all views as well as the average GLS compared with baseline measurements (-18.7±1.72 vs -15.15±1.76, p<0.001). This improvement was sustained at follow-up after 1 months with significant improvement compared with both the pre-BMV values (-20.75±1.92 vs -15.15±1.76, p<0.001) and the immediate post-BMV values(-20.75±1.92 vs -18.7±1.72, p<0.001) (Table 10). There was progressive trend towards normalization of the LV GLS values compared with the control group measurements during follow-up. There was also significant improvement in RV GLS compared with baseline measurements (-23.4±2.62 vs -17.55±2.54, p<0.001). This improvement was sustained at follow-up after 1month with significant improvement compared with both the pre-BMV values (-26.65±2.92 vs -17.55±2.54, p<0.001) and the immediate post-BMV values (-26.65±2.92 vs -

23.4±2.62, p<0.001), table (10). There was also progressive trend towards normalization of the RV GLS values compared with the control group measurements during follow-up (Figure 5). The LV average GLS showed modest but significant positive correlation with mean pressure gradient across mitral valve (MPG; r= 0.5, P = 0.006) and right ventricular systolic pressure (RVSP; r =0.6, P ¼ 0.005), and modest but significant inverse correlation with MVA by planimetry (r =20.4, P = 0.04. The RV GLS showed strong highly significant correlation with RVSP (r = 0.7, P 0.001) and modest but significant correlation with the MPG across the mitral valve (r = 0.6, P= 0.001). This study is the first study to evaluate the CS in patients with MS and the effect of BMV on it. We choose LV-CS on the MV level as it may be the most affected one (**nearest segments to the MV leaflets**). There was significant decrease of CS in patients with MS compared with control group(-17.05±2.7 vs -27.65±5.67, P<0.001) (table 5). Immediately after BMV, there was significant improvement in LV CS global and segmental compared with baseline measurements (-17.05±2.7 vs -21.9±2.83, p<0.001). This improvement was sustained at follow-up after 1 month with significant improvement compared with both the pre-BMV values (-23.75±2.2 vs -17.05±2.7, p<0.001) and the immediate post-BMV values (-23.75±2.2 vs -21.9±2.83, p<0.001)(table10). Further assessment of this function is of importance in order to assess the CS in patients with MS in the 3 levels of the short axis (MV level, papillary muscle level & apical level). We were expecting that CS of the LV which is a part of the LV function will try to compensate the decrease in LV LS, but this does not occur. In order to test an underlying myocardial factor for this decrease, this study compared regional LV longitudinal strain in the study group vs. control group. The presence of significant decrease in LV basal and mid-segmental strain values compared with control group and less or non-significant decrease in some apical segments (apical inferior, apical anterior septum & apical infero-septum) point out to possible underlying myocardial factor where rheumatic endocarditis and scarring extend from the mitral annulus to the surrounding LV segments; an effect that fades away as we go towards the apical segments. As our study found that the rest of other apical segments is affected and have lower segmental LS for example for apical anterior in study group compared to control group (-9.35±2.7 vs -19.45±2.39, p<.001), this may decline the thinking of rheumatic endocarditis and scarring may be the cause of subclinical affection. This myocardial factor could be the cause of incomplete improvement of the GLS after BMV and act as a contributing factor to the main effect of preload reduction in patients with MS on

GLS. Immediately after BMV, there was significant improvement of LV GLS compared with the same measurements before BMV (-15.15±1.76 vs 20.95±1.43, P<0.001). We demonstrated the presence of modest but significant correlation between LV GLS and indicators of success post-BMV, namely MPG (r = 0.5, P= 0.006) and RVSP (r=0.6, P= 0.005), and modest but significant inverse correlation with MVA by planimetry (r=20.4, P=0.04 and r=20.5, P= 0.005). In addition, this study showed a trend towards normalization of LV GLS compared with the control group after follow-up period of 1 months (-20.75±1.43 vs. -20.95±1.92). Whether this trend will continue on long-term follow-up till the complete normalization of these measurements or the suspected underlying myocardial factor will prevent these variables from complete normalization will need longer term follow-up. This study also found reduced RV GLS in patients with MS compared with controls (-23.4±2.62 vs -17.55±2.54, p<0.001). This study also demonstrated difference in regional RV longitudinal strain, there was significant decrease in the RV strain values of the septal segments, and basal RV free wall but there was no significant difference between the mid and apical RV free wall segments and those of the control group. This difference in the septal segments may point out to possible underlying myocardial factor where the rheumatic endocarditis and scarring extend from the mitral annulus to the surrounding LV segments and thus reflecting changes actually also occurring in the LV septum and affecting the mid & basal segments of the RV side. Our study found that segmental LS of the basal RV free wall is decreased compared to control group) -16.4±3.53 vs -22.25±2.1, p<0.001)this may be due to that the selected patients might have mild rheumatic TV affection undetected which affect basal RV free wall and affect also the basal septum of the RV. Most of the patients in our study have TR of varying degrees which is common than TS in rheumatic TV affection. Our study also found that apical segments (septal & RV free wall) have normal segmental LS in the patients group and even have higher LS compared to control group. This may be due to compensatory increase in their LS, may be due to increase in RVSP. Immediately after BMV, there was significant improvement of the RV GLS compared with the RV GLS before BMV (-19.35±2.54 VS 17.55±2.54, p<0.001). All septal segments and basal RV free wall have shown improvements immediately and after 1month. This improvement could be due to the improvement in the RV afterload as a result of the relief of the LV inflow obstruction. There was significant correlation between the RV-GLS and both MPG (r = 0.6, P= 0.001) and RVSP (r = 0.7, P = 0.0001) which again points out to the role of BMV in the relieve of the LV inflow obstruction and

consequently the decrease in the RV afterload which represent a major contributing factor in the improvement of the RV GLS. This study showed significant improvement of RV GLS compared with the control group immediately after BMV (-23.40± 2.62% vs. - 19.35± 2.54) which continued at follow-up after 1 month (-26.65+ 2.92% vs. -19.35± 1.3). We believe that this improvement is directly related to the significant reduction in both RV volumes as well as RV systolic pressure post-BMV.

Study limitations and recommendations

The extensive exclusion criteria applied to the patients before enrolment in the study may suggest that the population is not a real-world population. The main objective of this extensive exclusion criteria was to try to document the presence of subtle changes in LV and RV systolic functions related to MS and not to any other disease process and to test the effect of BMV on these changes. Correlation of decreased LV GLS in MS patients and future development of LV systolic dysfunction defined as EF ≤54%. Using longer-term studies should be considered. Such a correlation if proved together with the presence of subclinical affection of LV function in patients with MS and the significant sustained improvement in GLS of LV & RV also CS during short-term follow-up post-BMV proved in this study should have their impact on the current guidelines for BMV, so that we may consider in the future BMV for patients with impaired LV GLS in order to protect these patients from developing progressive LV systolic dysfunction. Also we recommend further study of the CS of LV in order to detect subclinical affection in patients with MS.

Conclusions

2D strain represents an evolving technique to identify subclinical LV and RV systolic dysfunction. This study represents the first attempt to study both LV and RV 2D strain and CS in the same group of patients with MS and to follow-up these patients after successful BMV. There was a significant decrease in both LV and RV GLS as well as CS compared with control group, a decrease which showed significant improvement in the immediate and short-term follow-up after BMV. We strongly support a mixed etiology theory involving both an. underlying myocardial as well as hemodynamic factor for subclinical affection of both RV and LV functions in patients with MS. The presence of significant difference in the regional strain values of both LV and RV segments and CS compared with control group points out to a myocardial factor, whereas the significant improvement in the RV and LV GLS and CS post-BMV underlines the important role of a hemodynamic factor in this improvement.

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