Changes in Left Ventricular Global Longitudinal Strain Before and After Balloon Mitral Valvuloplasty

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Abstract

Background: Several studies have reported left ventricular systolic dysfunction as measured by the global longitudinal strain (GLS) in patients with mitral stenosis. This study aims to determine left ventricular systolic function changes using global longitudinal strain early after balloon mitral valvuloplasty (BMV) and on long-term observation.

Methods: Baseline echocardiography data and GLS were taken before BMV, followed up early after (2 to 7 days), and in the long-term (6 months to 1 year) after BMV.

Result: Among 36 patients, the mean age was 43.41 ± 10.04 y.o, female dominant (72%); the majority have atrial fibrillation (56%), with a median mitral valve area (MVA) before BMV of 0.6 (0.2-1.3) cm² and mean mitral valve gradient before BMV of 12.95 ± 5.29 mmHg. GLS increased from $-14.34 \pm 3.05\%$ to $15.84 \pm 3.11\%$ and increased further to $-17.29 \pm 2.80\%$ ($p < 0.05$), at pre-BMV- early post-BMV, and long-term follow up, respectively.

Conclusions: There is a significant improvement in LV GLS early after BMV compare to baseline. The GLS improved further at long-term evaluation (six months until one year) after BMV.

Introduction

Mitral stenosis (MS) is the most common valve lesion in patients with rheumatic heart disease (RHD). Previously known that MS does not impose hemodynamic alterations on the left ventricle, therefore left ventricular (LV) dysfunction is uncommon in patients with MS [1]. However, several studies have reported that the mitral valve has subclinical left ventricular systolic dysfunction even with a normal ejection fraction [2–4].

Several mechanisms have been postulated to explain LV systolic dysfunction in patients with MS, including LV underfilling, chronic inflammation leading to abnormal wall motion owing to endomyocardial fibrosis, subvalvular apparatus scarring leading to wall motion abnormalities, reduced LV compliance, increased afterload leading to remodeling, abnormal right-left septal interaction from pulmonary hypertension, and concomitant diseases such as systemic hypertension and coronary artery disease [5].

Several studies have shown that early after balloon mitral valvuloplasty (BMV), the intrinsic LV systolic function improved, as measured by global longitudinal strain (GLS) using speckle tracking echocardiography (STE) [1, 6–8]. However, complete normalization of LV systolic function was not attained in those studies. A longer follow-up is needed to assess LV systolic function using GLS in MS patients. The objective of this study was to assess LV systolic function measured by GLS using STE before BMV, early after, and long-term observation after BMV.

Material And Methods

This is a pre-post study conducted at the National Cardiovascular Center Harapan Kita from April 2020 to April 2021. Patients aged >18 years with severe rheumatic MS suitable for BMV were included in this study. Patients with concomitant coronary artery disease (CAD), congenital heart disease, diabetes mellitus (DM), hypertension, any significant aortic valve abnormalities, significant mitral regurgitation, LV systolic function impairment, failed BMV were excluded from this study. Institutional review board approval was approved prior to enrollment, with written informed consent obtained from all patients.

Echocardiographic examinations were done using the General Electric Vivid E9 System (GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5 MHz transducer. All data were analyzed in a workstation (EchoPAC PC; GE Vingmed Ultrasound AS). Standard 2D and M- Mode echocardiograms were obtained according to the American Society of Echocardiography guidelines. Basic measurements included left ventricle end-diastolic volume (LVEDV), left ventricle end-systolic volume (LVESV), left ventricle ejection fraction (LVEF) by Simpson's rule, left atrial volume index (LAVi), tricuspid annular plane systolic excursion (TAPSE), and tricuspid regurgitation velocity maximum (TR Vmax) [9]. The assessment of the MS severity includes Mitral valve area (MVA) by 3D planimetry and pressure half-time (MVA PHT), and the mean mitral valve pressure gradients (MVG) were measured as recommended [10]. Left ventricular dysfunction was defined as $LVEF \leq 50\%$ Failed BMV was defined as post-BMV MVA $<1.5 \text{ cm}^2$ or less than twice of the baseline MVA and/ or moderate to severe mitral regurgitation after BMV)

Strain imaging of 2D speckle tracking echocardiography images was obtained and reported as the average of peak longitudinal strain of all segments obtained from LV apical 4-chamber, apical long axis, and apical 2-chamber views. All images were taken during breath holding at end-expiration format for 3 to 5 consecutive cycles. The frame rate for images was between 50 and 90 frames/s, the endocardial border was then determined manually, and the software system then created an automatic epicardial tracing for each view. Inadequate tracking segments were automatically excluded, and the investigator was able to correct the contour manually to achieve optimal tracking. Only segments with optimal tracking quality were included. All images were evaluated by one experienced cardiologist who was blinded to patient clinical characteristics. In addition, transthoracic echocardiography was also performed along with speckle tracking echocardiography before BMV, 2-7 days, and 6-12 months after BMV.

Statistical Analysis

A continuous variable was presented as mean $\pm$ standard deviation in normally distributed and median (interquartile range) in non-normally distributed data. The results of echocardiographic examination before, early after, and long-term evaluation after BMV were analyzed using two-tailed paired t-test. Correlation among different echocardiographic parameters was assessed using Pearson's correlation coefficient. The statistical analyses were performed using SPSS for Mac (Ver 26.0, IBM, New York). A p-value less than 0.05 was considered statistically significant.

Results

There were 103 patients who underwent BMV from April 2020 to April 2021. We included 36 patients in the study (**Supplementary Fig. 2**). They were predominated by females, and the mean age was 43.05 ± 9.89 years. The basic characteristics of the study subjects can be seen in Table 1. **Fig. 1** illustrates the comparison of global longitudinal strain by 2D STE before BMV, 2 -7 days after balloon mitral valvuloplasty, and 6 -12 months after balloon mitral valvuloplasty

Table 1. Basic Characteristics of Research Subjects

Variable	n = 36
Gender	10 (28)
Male, n (%)	26 (72)
Female, n (%)	
Age, years	43.41 ± 10.04
BMI (kg/m²)	$22.76 \pm (3.91)$
Rhythm	
Atrial fibrillation, n (%)	20 (56)
Sinus rhythm, n (%)	16 (44)

BMI Body Mass index, *BMV* Balloon Mitral Valvuloplasty

After BMV, the LVEDV, LVESV, and TAPSE were increasing, and the LAVI was decreasing, while the LVEF did not show any changes. Unlike LVEF, the GLS showed significant improvement during the follow-up period compared to baseline. The detailed changes of the echocardiographic parameters during each period of follow-up are shown in Table 2.

Table 2

Changes in Echocardiographic Parameters Before BMV, Immediately After BMV (2-7 days), and Long-term (6 months-1 years) after BMV

Echocardiographic variables	Group			Differences between groups		
	Before BMV	Immediately after BMV	Long term after BMV	P1	P2	P3
LVEDV, mL	69.67±19.93	87.72 ±20.10	93.19 ± 21.68	<0.001	0.05	<0.001
LVESV, mL	30.39 ± 9.76	37.44 ± 9.03	39.36 ± 10.49	<0.001	0.12	<0.001
LAVi m ²	103.75 ± 34.85	90.59 ± 35.27	75.84 (36-205)	<0.001	0.14	<0.001
TR Vmax m/s	3.36 (2.05-6.32)	2.72 ± 0.45	2.82 ± (1.6-3.6)	<0.001	0.28	<0.001
TAPSE, mm	19.2 ± 4.57	20.05 ± 4.07	21.72 ± 4.39	0.08	0.001	<0.001
MVG, mmHg	12.96 ± 5.29	4.65 ± 1.59	5.0 ± (3.2-1.0)	<0.001	0.001	<0.001
MVA Planimetry, cm ²	0.6 (0.2-1.3)	1.47 ± 0.29	1.46 ± 0.29	<0.001	0.32	<0.001
LVEF, %	57.28 ± 3.84	57.81 ±3.84	57.80 ± 3.46	0.44	0.10	0.06
GLS (%)	-14.34±3.06	-15.84 ±3.11	-17.29 ± 2.81	<0.001	0.002	<0.001
<i>BMV</i> Body Mass index, <i>BMV</i> Balloon Mitral Valvuloplasty, LV left ventricular, EDV end diastolic volume, ESV end systolic volume, LAVi left atrial volume index, TR Vmax tricuspid regurgitation velocity maximum, TAPSE tricuspid annular plane systolic excursion, MVG mitral valve gradient, MVA mitral valve area, EF ejection fraction, GLS global longitudinal strain, P1= Comparison between before BMV and immediately after BMV, P2= Comparison between immediately after BMV and long term after BMV, P3 = comparison between before BMV and long term after BMV						

We attempted to identify the correlates of the increment in GLS before BMV to immediately after BMV (**Table 3**) and also the increment in GLS immediately after BMV and long term after BMV (**Table 4**) with hemodynamic variables from echocardiography. No association was found between changes in GLS with changes in hemodynamic variables from echocardiography.

Table 3

Correlation between GLS changes and other hemodynamic changes, before and immediately after BMV

Variable	Δ GLS	
	r	p-value
Δ LVEDV	0.16	0.343
Δ LVESV	0.24	0.154
Δ LAVI	0.11	0.510
Δ TR Vmax	-0.15	0.397
Δ MVG	-0.29	0.084
Δ MVA Planimetry	0.12	0.504
Δ LVEF	-0.23	0.186
<i>LV</i> left ventricular, <i>EDV</i> end diastolic volume, <i>ESV</i> end systolic volume, <i>LAVi</i> left atrial volume index, <i>TR Vmax</i> tricuspid regurgitation velocity maximum, <i>TAPSE</i> tricuspid annular plane systolic excursion, <i>MVG</i> mitral valve gradient, <i>MVA</i> mitral valve area, <i>EF</i> ejection fraction, <i>GLS</i> global longitudinal strain.		

Table 4

Correlation between GLS improvement and other hemodynamic changes, immediately and long-term after BMV

Variable	Δ GLS	
	r	p-value
Δ LVEDV	-0.23	0.17
Δ LVESV	-0.28	0.09
Δ LAVI	-0.16	0.35
Δ TR Vmax	-0.09	0.6
Δ MVG	-0.07	0.69
Δ MVA Planimetry	0.25	0.14
Δ LVEF	-0.23	0.18
<i>LV</i> left ventricular, <i>EDV</i> end diastolic volume, <i>ESV</i> end systolic volume, <i>LAVi</i> left atrial volume index, <i>TR Vmax</i> tricuspid regurgitation velocity maximum, <i>TAPSE</i> tricuspid annular plane systolic excursion, <i>MVG</i> mitral valve gradient, <i>MVA</i> mitral valve area, <i>EF</i> ejection fraction, <i>GLS</i> global longitudinal strain.		

Discussion

The current study aimed to observe any changes in intrinsic LV systolic function by GLS after BMV in rheumatic MS. We found that in our patients with successful BMV, there was a continuous improvement of the LV GLS until six months to 1 year of follow-up compared to baseline, which was not found in the LVEF. It supports other studies which suggest that the LVEF is less sensitive to evaluate LV function when compared to GLS. [11] To the best of our knowledge, this is the first study to assess subclinical LV function using GLS in rheumatic MS patients and to evaluate GLS immediately after BMV and 6-12 months after BMV.

Although at baseline, all of our patients had relatively normal LVEF ($57.28 \pm 3.84\%$), there was a significant reduction in LV GLS ($-14.34 \pm 3.06\%$). This finding is similar to some reports of the previous studies [1, 6–8]. There are some hypotheses that explain the presence of LV systolic dysfunction in rheumatic MS. In the initial attack of rheumatic carditis, all three layers of the heart may involve. [12] Chronic inflammation may then occur, leading to fibrosis and scarring of the myocardial and subvalvular apparatus. This “myocardial factor” may cause wall motion abnormalities [4]. Another study also suggests a contribution of the “hemodynamic factors,” include: LV filling reduction, reduced LV compliance, increased afterload, and abnormal septal interaction due to pulmonary hypertension [5]. Further study is needed to understand the true mechanism causing the LV dysfunction in rheumatic MS.

Early after BMV, we found that LV GLS increased significantly compared to baseline, from $-14.34 \pm 3.06\%$ to $-15.84 \pm 3.11\%$, respectively. Similar findings were also reported by several studies. [1, 6–8]. In our study, no correlation was found between changes in GLS early after BMV with changes in hemodynamic variables from echocardiography (LVEDV, LVESV, LAVi, TRVmax, MVG, and MVA) in contrast to previous studies [1, 6–8]. After 6-12 months of follow up, even though there were insignificant changes in hemodynamic echocardiography parameters, we found that compared to early after BMV, the LV GLS was improving further significantly, with GLS -15.84 ± 3.11 to $-17.29 \pm 2.81\%$, respectively and there was still no correlation was found between changes in GLS long-term after BMV with hemodynamic echocardiography parameters. Our study suggested that improvement on hemodynamic factors or loading conditions were less likely to contribute to the improvement of GLS early after BMV nor in the long-term after BMV.

A plausible explanation is that other than the amount of diastolic filling, how the ventricle is filled also affects LV systolic function. [13, 14]. In a normal heart, the flow follows a certain sequence of spiral rings or vortices; this special pattern of filling is important to maintain systolic and diastolic performance [15]. The BMV may alter the ventricle filling, which might be associated with the continuous improvement of GLS, but unfortunately, how the ventricle is filled is not explored in our study, so it needs a further study to prove it.

Another hypothesis suggests a process analogous to stunning -as in coronary artery disease- may occur in post BMV. Stunning myocardium in coronary artery disease is viable myocardium salvaged by coronary reperfusion that exhibits prolonged post-ischemic dysfunction after reperfusion. [15] Reperfusion precipitates a burst of reactive oxygen species formation and alterations in excitation-

contraction coupling, which interact and cause contractile dysfunction. [16] There is a gradual recovery of contractile function after reperfusion on myocardial stunning. For MS patients, BMV could be analog to “reperfusion” as in coronary artery disease, and it might induce reactive oxygen and cause LV dysfunction, so it required some time for LV to recover, as could be seen with gradual improvement on GLS after BMV in our study. However, it needs further study to prove those hypotheses.

This study provides answer to limitation from previous similar studies regarding whether a longer follow-up period normalized GLS. Our study showed that even though GLS improved when the follow-up period was extended until one year after BMV, it still has not reached the normal values. We suspect that myocardial factors may prevent the normalization of GLS in MS patients. A study by Rousdhy *et al.* and Mahajan *et al.* showed that the GLS in the basal segment is much lower than the mid and apical segment; this may be due to the formation of fibrotic tissue due to the rheumatic process of endocarditis that started from mitral annulus extending to basal segment and decreased as it approached the apical segment [7, 1]. A study by Soesanto *et al.* proved that myocardial factor is also associated with LV dysfunction in rheumatic MS, as a significant negative correlation between GLS and late gadolinium enhancement on MS patients was found, suggesting a higher degree of fibrosis and worse LV systolic dysfunction [17]. A longer follow-up is also needed to prove a further improvement in GLS.

Study Limitations and Recommendations

There are several limitations to this study. We did not compare the GLS in our subjects with the MS population who did not undergo BMV. However, a study by Mehta *et al.* found that no significant changes in GLS were found in MS patients who did not undergo BMV at 1-month follow-up. The number of patients lost to follow-up was quite large due to the COVID-19 pandemic, although the target study sample was achieved in the end. The high prevalence of AF in this study may have affected measurements, even though care has been taken to avoid unreliable data. Another limitation is that diagnosis of coronary artery disease was based only on the patient history obtained from the electronic medical record, symptoms, and electrocardiography. We did not perform cardiac catheterization or coronary multislice computed tomography.

Further studies with a longer duration of follow-up are needed to assess whether GLS improvement will sustain. It is necessary to conduct a study to explore the relationship between intrinsic ventricular systolic dysfunction as measured by GLS and its changes after BMV with clinical importance such as treatment and prognosis.

Conclusions

There was a significant improvement in intrinsic LV systolic function as assessed by GLS in rheumatic MS patients early after BMV. This improvement can be observed continuously until 6-12 months follow-up.

Abbreviations

BMV : balloon mitral valvuloplasty

CAD : coronary artery disease

GLS : global longitudinal strain.

LAVi : left atrial volume index

LV : left ventricular

LVEDV : left ventricle end-diastolic volume

LVEF : left ventricular ejection fraction

LVESV : left ventricle end-systolic volume.

MS : mitral stenosis

MVA : mitral valve area

MVA PHT : mitral valve area pressure half time

MVG : mitral valve pressure gradients

RHD : rheumatic heart disease

STE : speckle tracking echocardiography

TAPSE : tricuspid annular plane systolic excursion

TR Vmax : tricuspid regurgitation velocity maximum

Declarations

Compliance with ethical standards

Conflict of interest. All authors declare that there are No. conflicts of interest.

Ethical approval. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards as reflected in a priori approval by the National Harapan Kita Cardiovascular Centre Institutional Review Board.

Informed consent. Informed consent was obtained from all individual participants included in the study.

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Figures

Figure 1

Measurement of global longitudinal strain before balloon mitral valvuloplasty (a) 2-7 days after balloon mitral valvuloplasty (b) 6-12 months after balloon mitral valvuloplasty (c)

Supplementary Files

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