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Left Ventricular Mechanics in Isolated Rheumatic Mitral Stenosis; Impact of Loading Condition on Different Parameters of the Left Ventricular Function

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ABSTRACT

Background: Rheumatic mitral stenosis leads to depressed ventricular function, which is not detectable through the measurement of ejection fraction. Whether pancarditis or changes in loading condition results in subclinical Left Ventricular (LV) dysfunction has yet to be fully elucidated.

Objectives: The aim of this study is to evaluate the effect of loading condition on left ventricular function.

Methods: The present observational, case-control study was conducted on 104 cases who were referred to the echocardiography department including 71 patients with different severity degrees of rheumatic mitral stenosis and 33 healthy individuals with no past history of cardiac or other medical illnesses and with normal echocardiography who were matched with the cases in terms of age, gender, and body surface area. The strain, strain rate, rotation, torsion, and twist parameters of the left ventricle were measured via 2D speckle-tracking echocardiography. The data were analyzed using Kolmogorov–Smirnov test, independent student t-test, and one-way Analysis of Variance (ANOVA), as appropriated. Correlation analysis was also performed using linear regression, and the results were expressed as Pearson's correlation coefficients.

Results: The LV Global Longitudinal Strain (GLS), Global Longitudinal Strain Rate (GLsr), and Global Circumferential Strain Rate (GCsr), but not Global Circumferential Strain (GCS), basal and apical rotations, twist, and torsion, were significantly lower in the subgroup with progressive mitral stenosis (17.7%, 1.07s-1, 22.85%, and 1.05s-1 , respectively) compared to the healthy group (19.76%, 1.17 s-1, 24.15%, and 1.27 s-1, respectively) (P = 0.001, 0.032, 0.104, and < 0.001, respectively). Increase in the severity degree of mitral stenosis was accompanied by a significant decrease in the mentioned parameters.

Conclusions: The rheumatic process led to a reduction in ventricular function, which was detectable through the measurement of the GLS, GLsr, and GCsr, but not GCS, twist, rotation, and torsional parameters of the left ventricle. As the severity of the stenosis progressed, other indices of the LV function such as rotation, twist, and torsion decreased significantly, indicating their more susceptibility to loading conditions compared to the rheumatic process per se.

1. Background

The rheumatic inflammatory process continues to be the leading cause of Mitral Stenosis (MS) in developing countries. An increase in the severity of MS begets a meaningful drop in the Left Ventricular (LV) preload. Since the LV function is determined by the interactions among the myocardial tissue architecture, myocardial contractility, preload, and afterload (1), myocardial performance would change theoretically. Deterioration in the LV systolic function has been previously reported in a fraction of

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patients with mild MS in the absence of a low preload (2). It has also been reported among patients with various degrees of MS that reduced LV function is not detectable through the measurement of Ejection Fraction (EF), but via 2D strain imaging that is independent of the hemodynamic severity of MS (3). Intrinsic myocardial dysfunction has been deemed an important etiology for myocardial dysfunction. Nonetheless, what the existing literature lacks despite such valuable data is evidence regarding all aspects of the LV mechanical function including the strain rate, strain, twist, and torsion in patients suffering from different severity degrees of MS.

Speckle tracking echocardiography is a quantitative ultrasound technique for accurate evaluation of the LV systolic function via tracking the displacement of the speckles and offline measurement of strain and strain rate (4). Twist and torsion are other non-invasive techniques for understanding the LV mechanics in clinical settings and are useful for clinical differentiation of LV dysfunction in daily practice (5). These newer modalities can detect subclinical LV dysfunctions, which are not detectable by measurement of EF.

2. Objectives

The present study aims to assess the alterations in the aforementioned LV function markers among patients with any degree of MS severity to determine whether pancarditis caused by rheumatic inflammation or changes in preload can result in subclinical LV dysfunction.

3. Materials and Methods

3.1. Study Population

The present observational, case-control study was conducted in Shariati Hospital and Rajaie Cardiovascular Medical and Research Center, Tehran, Iran from March 2019 to March 2020. A total of 75 patients with the mean age of 33.11 years with a diagnosis of rheumatic MS with any degree of severity who were referred to the echocardiography department for routine echocardiography were enrolled into the case group, and 40 healthy individuals with the mean age of 30.66 years with no previous history of heart problems, normal resting ECG and echocardiography, and no history of hypertension, diabetes, and diseases in other organs were assigned to the control group. The two groups were matched in terms of age, gender, and body surface area. Patients with hypertension, diabetes mellitus, rhythms other than the normal sinus rhythm, moderate-to-severe stenosis, regurgitation of other valves, more than mild pericardial effusion, history of coronary artery disease or wall motion abnormalities, history of chronic obstructive lung disease, history of cardiac surgeries, EF < 50% at baseline, and images with poor quality were excluded from the study. It should be noted that all data were anonymized.

Based on the 2014 recommendations of the American Heart Association/American College of Cardiology, severe MS was defined as a mitral valve area of less than 1.5 cm2, progressive MS as a minimum mitral valve area of 1.5 cm2, and very severe MS as a mitral valve area of less than 1cm2 in 3D direct planimetry (6). The LV function parameters, namely strain, strain rate, rotation, twist, and torsion, were measured offline using a Philips EPIQ 7C echocardiography machine.

Written informed consent was obtained from all patients and the study was approved by the local Ethics Committee of the institute.

3.2. Echocardiography Image Acquisition

All echocardiographic examinations were performed while the patients were at resting position using a Philips EPIQ 7C medical system with S5 broadband phased-array transducers. First, a 2D echocardiographic examination was performed to exclude any abnormalities with regard to the wall thickness, chamber size, and cardiac function as well as any significant valvular dysfunctions other than MS.

In the center under investigation, echocardiographic parameters are measured in accordance with the recommendations of the American Society of Echocardiography (7). In the present study, the LV end-diastolic and end-systolic diameters and the LV wall thickness were measured in the parasternal long-axis view at the level of the chordae tendineae. In addition, the Right Ventricular (RV) diameter was measured in the RV focused view at the tip of the tricuspid valve in end diastole. Pulmonary artery pressure was assessed by derivation of RV pressure from the tricuspid regurgitation velocity added to right atrial pressure. In order to measure the LV volume and LVEF, 3D Echocardiography (3DE) data were achieved by a matrix array transducer as well as electrocardiography triggered 3-beat data acquisition from a transthoracic apical window. To reduce the imaging artifact, 2D images were optimized. Both gain and compression were set at the midrange (50 units) and, if needed, were optimized more via Time Gain Compensation. The patients were required to hold their breaths in order to reduce stich artifact. Land marks were put in the mitral annulus and LV apex to initiate edge detection. LV trabeculation and papillary muscles were included within the LV cavity while trying to reduce forshortening, malrotation, and angulation. The QLab 3D quantification software algorithm was employed for edge detection and data calculation.

Gray-scale digital cine-loop images for 2D speckle-tracking echocardiography were acquired at 60 - 90 frames per second during three consecutive beats triggered to the QRS complex. With the aid of the 2DQA application in the apical view, the end-diastolic reference points were placed in the 4-, 2-, and 3-chamber views, the septal and lateral reference points in the 4-chamber view, the anterior and inferior reference points in the 2-chamber view, and the anteroseptal and posterior reference points in the 3-chamber view. The software automatically tracked each view throughout the cardiac cycle. The tracking quality was verified, and manual adjustments were made if the tracking was not satisfactory so as to ensure that most of the wall thickness was under analysis and that the pericardium was avoided. The LV Global Longitudinal Strain (GLS) and Global Longitudinal Strain Rate (GLsr) were calculated by analyzing three apical long-axis views. Additionally, the LV Global Circumferential Strain (GCS) and Global Circumferential train Rate (GCsr) were calculated by analyzing three parasternal short-axis views. The apical

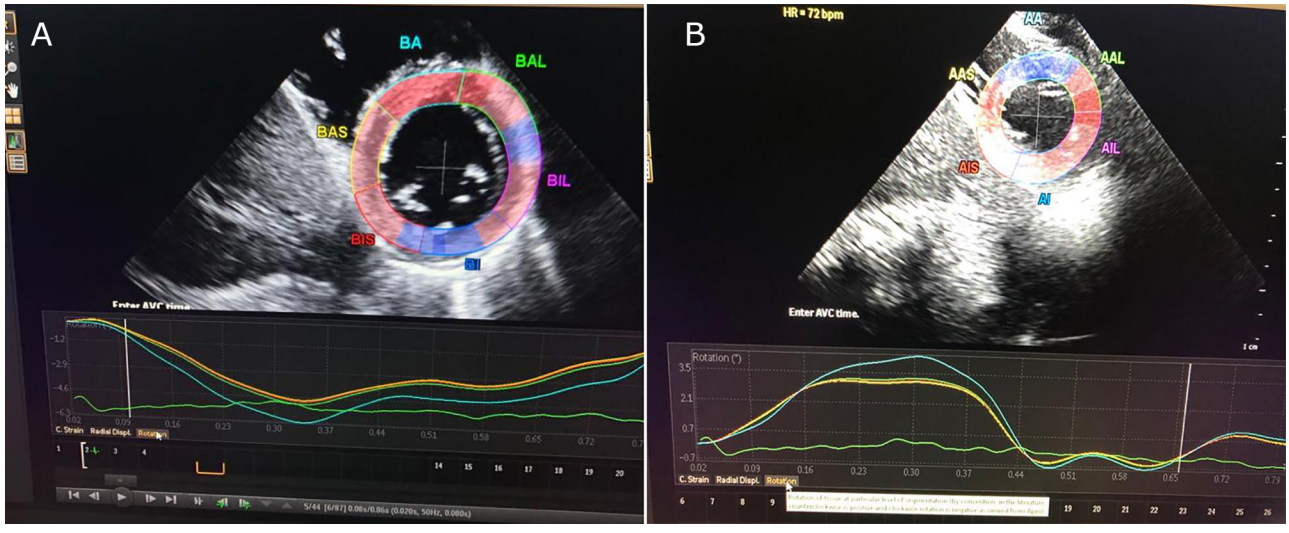

Figure 1. Basal (A) and Apical (B) Rotations of the Left Ventricle. The Basal Rotation is a Negative Value and the Apical Rotation is a Positive Value.

rotation was calculated as the peak counterclockwise rotation of the short axis of the LV apex, as viewed from the apex, and was expressed as a positive value. The basal rotation was calculated as the peak clockwise rotation of the LV base and was expressed as a negative value. The LV twist was calculated as the peak net difference in the systolic rotation between the apex and the base. The LV torsion, which is a normalized twist, was calculated through the division of the twist angle by the distance between the measured locations of the base and the apex (Figure 1) (1, 8, 9).

The inter- and intra-observer variabilities of the measurements were assessed in 15 randomly selected patients to validate the data. The inter-observer variability was assessed through the remeasurement of the data by the first operator with a one-month interval, while the intra-observer variability was assessed via the remeasurement of the data by the second operator who was blinded to the results of the first measurement.

3.3. Statistical Analysis

The nominal data were presented as number (%), while the continuous data were expressed as mean ± Standard Deviation (SD). Inter-observer variability analysis was performed using intra-class correlation coefficients for longitudinal and circumferential strains, revealing the variabilities of 5% and 4%, respectively. The normality of the variables was tested using Kolmogorov–Smirnov test. Then, parametric and non-parametric continuous variables were compared using independent student t-test or one-way Analysis of Variance (ANOVA). Moreover, correlation analyses were performed using linear regression and the results were expressed as Pearson's correlation coefficients. All data analyses were carried out using the SPSS 22 software (SPSS Inc., Chicago, IL) and $P < 0.05$ was considered significant. It is worth noting that the authors had full access to the data and take full responsibility for their integrity.

4. Results

The study population consisted of 104 participants (90 females and 14 males) divided into an MS group (n = 71) and a healthy group (n = 33). The mean age of the participants was 32.28 ± 8.63 years. The results showed no significant difference between the two groups concerning age (P = 0.281), gender (P = 0.061), and the body surface area (P = 0.072). The demographic data of the study population have been depicted in Table 1.

The study population's conventional echocardiographic data have been presented in Table 2. Accordingly, the LV end-diastolic diameter was significantly larger in the healthy participants compared to the patients (P = 0.032). The LV end-diastolic diameter was also significantly larger in the healthy controls in comparison to the patients with different severities of MS (P = 0.033, 0.030, and 0.034 in patients with progressive, severe, and very severe MS, respectively). However, no significant difference was observed between the MS group and the healthy group regarding other indices of the left ventricle; i.e., LV end-systolic and end-diastolic diameters and end-systolic volume, RV size; i.e., RV end-diastolic diameter, and LVEF (P = 0.641). Increase in the

Table 1. The Demographic Data of the Healthy Individuals and the Patients with Different Severity Degrees of MS

	Total (n=104)	Progressive MS (n=23)	Severe MS (n=34)	Very Severe MS (n=14)	Healthy (n=33)	P-value
Male, n (%)	14 (13.5)	0	4 (11.8)	3 (13)	7 (21.2)	0.061
Age (y)	32.28 (± 8.63)	34.57 (± 9.66)	33.85 (±8.62)	30.91 (±8.72)	30.66 (± 7.99)	0.281
Height (cm)	163.46 (± 7.24)	158.85 (± 3.89)	164.38 (±6.83)	162.91 (±6.45)	164.84 (± 8.58)	0.054
Weight (kg)	63.77 (± 9.57)	58.78 (± 7.11)	65.52 (±8.58)	64.26 (±9.20)	63.72 (± 11.23)	0.172
BSA (m^2)	1.67 (± 0.17)	1.57 (± 0.09)	1.70 (±0.17)	1.66 (±0.13)	1.69 (± 0.20)	0.072

Values have been expressed as mean (±SD) for quantitative variables and number (%) for qualitative ones. *One-way ANOVA with Bonferroni post-hoc and chi-square test were used.

Abbreviations: MS, mitral stenosis; BSA, body surface area.

Table 2. The Conventional Echocardiographic Data of the Healthy Individuals and Patients with Different Severity Degrees of MS

	Total (n = 104)	Very Severe MS (n = 14)	Severe MS (n = 34)	Progressive MS (n = 23)	Healthy (n = 33)	P-value
LVEDD (mm/m2)	28.02 (5 ± .31)	27.10 (± 5.09)	27.85 (± 5.19)	27.35 (± 6.07)	29.06 (± 5.03)	0.032 **
LVESD (mm/m2)	28.02 (± 5.31)	27.10 (± 5.09)	27.85 (± 5.19)	27.35 (± 6.07)	29.06 (± 5.03)	0.561
LVEF (%)	57.58 (± 3.63)	57.32 (± 3.63)	57.20 (± 3.67)	57.29 (± 3.76)	58.26 (± 3.58)	0.641
RVEDD (mm)	26.00 (± 4.18)	26.70 (± 4.09)	27.13 (± 4.14)	25.78 (± 3.88)	24.70 (± 4.27)	0.104
LAvolume /index (cm^2/m^2)	28.51 (± 6.93)	36.90 (± 4.19)	31.42 (± 6.63)	25.44 (± 5.85)	24.10 (± 3.51)	< 0.001 **
PAP (mm Hg)	34.09 (±11.27)	51.57 (±7.87)	39.15 (±9.41)	28.13 (±5.37)	25.63 (±3.52)	<0.001**
LVESV (mL/m2)	81.93 (±14.19)	75.55 (±10.41)	80.95 (±10.80)	83.25 (±13.23)	84.72 (±18.31)	0.217
LVEDV (mL/m2)	34.68 (±6.45)	32.08 (±4.46)	34.58 (±5.89)	35.23 (±5.96)	35.49 (±7.84)	0.402
MVA (cm^2)	1.36 (±0.42)	0.74 (±0.11)	1.26 (±0.18)	1.76 (±0.22)	-	<0.001**

Values have been expressed as mean (± SD) for quantitative variables.
Abbreviations: LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; RVEDD, right ventricular end-diastolic diameter; LA, left atrial; PAP, pulmonary arterial pressure; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume; MVA, mitral valve area.
**P-value<0 .05.

Table 3. Data on LV Rotation, Twist, Torsion, GLS, GLsr, GCS, and GCsr in the Healthy Individuals and Patients with Different Severity Degrees of MS

	Healthy (n = 33)	Progressive MS (n = 23)	P-value*
Basal rotation (degree)	-6.15 (± 0.90)	-5.35 (± 1.30)	0.008
Apical rotation (degree)	13.02 (± 1.98)	12.95 (± 1.52)	0.889
Twist (degree)	19.17 (± 2.41)	18.12 (± 2.52)	0.120
Torsion (degree/cm)	2.83 (± 0.59)	2.88 (± 0.67)	0.788
GLS (%)	19.76 (± 2.37)	17.17 (± 1.91)	< 0.001**
GLsr ($s^{-1)}$	1.17 (± 0.17)	1.07(± 0.18)	0.032**
GCS (%)	24.15 (± 3.00)	22.85 (± 2.69)	0.104
GCsr (s^{-1})	1.27 (± 0.22)	1.05 (± 0.19)	< 0.001**

Data have been presented as mean (± SD).
Abbreviations: LV, left ventricle; GLS, global longitudinal strain; GLsr, global longitudinal strain rate; GCS, global circumferential strain; GCsr, global circumferential strain rate.
**P-value < 0.05.

Table 4. Comparison of the Healthy Participants and Patients with Progressive MS Regarding 3D LV Rotation, Twist, Torsion, GLS, GLsr, GCS, and GCsr

	Healthy (n = 33)	Progressive MS (n = 23)	P-value*
Basal rotation (degree)	-6.15 (± 0.90)	-5.35 (± 1.30)	0.008
Apical rotation (degree)	13.02 (± 1.98)	12.95 (± 1.52)	0.889
Twist (degree)	19.17 (± 2.41)	18.12 (± 2.52)	0.120
Torsion (degree/cm)	2.83 (± 0.59)	2.88 (± 0.67)	0.788
GLS (%)	19.76 (± 2.37)	17.17 (± 1.91)	< 0.001**
GLsr ($s^{-1)}$	1.17 (± 0.17)	1.07(± 0.18)	0.032**
GCS (%)	24.15 (± 3.00)	22.85 (± 2.69)	0.104
GCsr (s^{-1})	1.27 (± 0.22)	1.05 (± 0.19)	< 0.001**

Data have been presented as mean (± SD).
Abbreviations: LV, left ventricle; GLS, global longitudinal strain; GLsr, global longitudinal strain rate; GCS, global circumferential strain; GCsr, global circumferential strain rate.
**P-value < 0.05.

severity of MS was accompanied by a significant increase in the left atrial volume and the systolic pulmonary arterial pressure (P < 0.001 and < 0.001, respectively).

The data on the LV mechanics, namely rotation, twist, torsion, GLS, GLsr, GCS, and GCsr, have been presented in Table 3.

The results revealed a significant difference between the MS and healthy groups regarding all aspects of the LV mechanics, except for torsion. For further assessments, the data were analyzed amongst the patients with progressive MS and the healthy individuals with a view to evaluating the effect of the rheumatic process (Table 4). Subsequently, the subgroups of MS were compared with regard to all these measurements so as to assess the effect of the loading condition (Table 5).

The results indicated that the basal rotation was lower in the MS group (P = 0.008), but the difference was not statistically significant (P = 0.491 between the severe and very severe groups). Moreover, the LV parameters of GLS, GLsr, and GCsr, but not GCS, were significantly higher in

Table 5. Comparison of the MS Subgroups Regarding 3D LV Rotation, Twist, Torsion, GLS, GLsr, GCS, and GCsr

	Progressive MS (n = 23)	Severe MS (n = 34)	Very Severe MS (n = 14)	P-value*
Basal rotation (degree)	5.35 (± 1.30)	3.96 (± 1.23)	3.16 (± 0.67)	< 0.001**
Apical rotation (degree)	12.95 (± 1.52)	10.73 (± 1.89)	9.58 (± 1.49)	< 0.001**
Twist (degree)	18.12 (± 2.52)	14.70 (± 2.43)	12.75 (± 1.58)	< 0.001**
Torsion (degree/cm)	2.88 (± 0.67)	2.38 (± 1.26)	2.06 (± 0.37)	0.040**
GLS (%)	17.17 (± 1.91)	16.89 (± 2.15)	17.86 (± 2.44)	0.365
GLsr (s^{-1})	1.07 (± 0.18)	1.04 (± 0.25)	1.11 (± 0.22)	0.561
GCS (%)	22.85 (± 2.69)	20.25 (± 2.95)	20.74 (± 2.47))	0.006**
GCsr (s^{-1})	1.05 (± 0.19)	1.07 (± 0.27)	1.09 (± 0.24)	0.902

Data have been presented as mean (± SD).
Abbreviations: GLS, global longitudinal strain; GLsr, global longitudinal strain rate; GCS, global circumferential strain; GCsr, global circumferential strain rate.
**P-value < 0.05.

Table 6. The Correlations between Twist, Torsion, GLS, and GCS Values and Echocardiographic Parameters

	Twist		Torsion		GLS		GCS	
	r	P-value	r	P-value	r	P-value	r	P-value
LVEF	0.223	0.025	0.212	0.034	0.112	0.266	0.142	0.156
LA volume	-0.612	< 0.001	-0.546	< 0.001	-0.365	< 0.001	-0.321	0.001
PAP	-0.675	< 0.001	-0.598	< 0.001	-0.388	< 0.001	-0.320	0.001
Mitral valve area	0.723	< 0.001	0.598	< 0.001	0.051	0.662	0.244	0.035

Pearson's correlation coefficient was used for determining the correlations between the variables.
Abbreviations: GLS, global longitudinal strain; GCS, global circumferential strain; PAP, pulmonary arterial pressure; LVEF, left ventricular ejection fraction; LA, left atrium.

the healthy individuals than in the patients with progressive MS (P < 0.001, 0.032, < 0.001, and 0.14 respectively). However, no significant difference was observed between the two groups concerning the apical rotation, twist, and torsion (P = 0.889, 0.120, and 0.788, respectively).

The results of comparison of the three subgroups of patients with MS in terms of LV rotation, twist, and torsion, GLS, GLsr, GCS, and GCsr have been illustrated in Table 5. Accordingly, disease progress and increase in MS severity from progressive to severe was accompanied by a decline in LV rotational parameters in the base and apex as well as in LV torsion and twist (P < 0.001, < 0.001, < 0.001, and 0.040, respectively). Nevertheless, such a decline was not evident after progression to very severe MS (P = 0.491, 0.273, 0.083, and 0.354, respectively). The results also showed no significant decrease in GLS, GLsr, GCS, and GCsr by disease progression (P = 0.721, 0.312, 0.641, and 0.854, respectively between severe and very severe groups).

The results of correlation analysis revealed moderate correlations between the left atrial volume and the pulmonary arterial pressure on the one hand and among twist, torsion, GLS, and GCS on the other hand. While there was a moderate correlation between LVEF and the LV twist and torsion, no correlation was found between LVEF and GLS and GCS. Furthermore, the mitral valve area had moderate correlations with twist, torsion, and GCS, but no correlations with GLS (Table 6).

5. Discussion

The world has experienced a reduction in the prevalence of rheumatic MS in the recent years, but the disease is still considered a major public health concern in developing countries. The contribution of MS to LV dysfunction has been known for several years (8-10). The first report of depressed myocardial function as interpreted by myocardial velocity via tissue Doppler imaging was published by Özdemir et al. in 2002 (11). They found significantly reduced myocardial velocities as the indicators of LV function. Subsequent research confirmed that finding with the aid of Doppler-derived strain and strain rate (12, 13). Moreover, some investigators reported deterioration in LV function despite the absence of a hemodynamic load imposed by stenotic valves (2)s. What has hitherto remained unknown, however, is whether subtle LV dysfunction, which is not detectable by calculating EF, is caused by the rheumatic process and the resultant pancarditis. Overall, myocardial function may be weakened as a result of chronic myocardial inflammation, scarring of the subvalvular apparatus, diastolic dysfunction, reduced LV compliance, increased afterload, abnormal right-left septal interaction, and pulmonary hypertension (14, 15).

For early detection of LV pump dysfunction, physicians should draw upon imaging and techniques other than EF calculation. These modalities include 2D- and 3D-based strain and strain rate, twist angle, rotation, and torsion. The systolic strain of the left ventricle has been defined as its shortening normalized to its original shape, which is expressed as a negative percentage. The LV strain rate refers to the change in its strain over time (16).

The myocardial fibers within the LV wall are oriented as a right-handed helix in the subendocardium that changes gradually to a left-handed helix in the subepicardium and becomes almost horizontal in the mid-wall. This complex helical architecture brings about the counterclockwise rotation of the LV apex and the clockwise rotation of the LV base during the contraction of the subepicardial fibers. The reverse is true for the subendocardial fibers. The large radius of the rotation of the epicardial layer

with the resultant higher torque results in the global counterclockwise rotation of the LV apex and the clockwise rotation of the LV base during ejection (17). This knowledge enables the measurement of some other aspects of the left ventricle, namely rotation, twist, and torsion. Basal rotation has been defined as the peak clockwise systolic rotation of the LV basal short axis, whereas apical rotation refers to the peak counterclockwise rotation of the apical short axis when both are viewed from the apex. The LV twist has been defined as the peak difference between the LV apical and basal rotations, while the LV torsion refers to the twist normalized by the distance between the measurement site and the apex (1).

Strain echocardiography is a novel tool for tracking myocardial speckle displacement in an angle-independent manner. All aforementioned aspects of the LV function are measurable by strain echocardiography, with GLS, twist, and torsion comprising the most widely used parameters. It is noteworthy that the stimulus that alters the LV preload, afterload, and contractility can alter its twist response (18). Lima et al. (19) directly compared these relatively novel parameters to LVEF and concluded that GLS had a stronger correlation with LVEF in comparison to twist and torsion. Furthermore, Poyraz et al. (2) evaluated 31 patients with mild MS and compared them to 27 healthy controls by collecting data on the LV basal strain, twist angle, and torsion via 2D and 3D strain echocardiography. They came to the conclusion that the patients with mild MS had lower GLS, GCS, and global rotational strain compared to the healthy group. In addition, they indicated no significant difference between the two groups regarding the LV twist, while torsion was significantly higher in the MS group. Overall, they reported that subclinical LV dysfunction could develop in the early stages of the disease. A reduction in the LV torsion and basal rotation in patients with MS was also documented by Kirilmaz et al. (20) in a study on 19 patients with isolated mild MS. This could be attributed to changes in the LV muscle cells involving the myofibrils, mitochondria, some elements of sarcoplasm, and the membranes of the myocardial cells, as described by Lee et al. (21) in an electron microscopic study of the LV myocardium in 1990. Another theory is the compensation of one parameter by another. Galli et al. (22) emphasized that the myocardium could be deformed in three dimensions simultaneously. As a result, the global LV function might remain normal despite the changes in myocardial deformation properties. In a previous study, a decrease shown by the longitudinal 2D strain analysis was more prominent in all basal and some mid segments of the left ventricle, whereas the apical segments were not significantly involved (23). In the present study, the healthy individuals and patients with mild MS were not significantly different with respect to the LV twist and torsion angles. Nonetheless, GLS was significantly lower in the subgroup with mild MS compared to the other two subgroups with MS and the healthy controls.

As the severity of MS progresses, the reduction in the LV twist and torsion becomes more prominent. It can thus be concluded that twist and torsion are not affected solely by the rheumatic process and are more load-dependent in contrast to GLS and GLsr that are affected in the early stages of the rheumatic process. Recently, Anwar Samaan et al. (24) evaluated the impact of Balloon Mitral Valvuloplasty (BMV) on the LV rotational deformation by utilizing tagging techniques in cardiac magnetic resonance imaging and detected a significant improvement in the median LV base/apex rotation following a successful BMV procedure. Accordingly, the preload could affect torsional parameters. Additionally, the effect of BMV and the resultant increase in preload could augment the peak LV annular velocity of systolic excursion in ejection and the peak annular velocity in early diastole and confer immediate improvements in LV function (15). However, contradictory results were subsequently reported by Rifaie et al. (25) who drew upon strain echocardiography to study 39 candidates for BMV. They assessed twist mechanics; i.e., basal rotation, apical rotation, and torsion, before and immediately after BMV and demonstrated exacerbated twist mechanics following BMV, which might be due to the failure of the left ventricle to adapt to the sudden rise in preload.

GLS in the right ventricle can be affected in patients with MS. Nevertheless, although the reduction in GLS occurs in the basal and mid segments of the septum, only lower strain values can be detected in the basal RV free wall (23). Since the septum is common between the right and left ventricles, it can be concluded that the reduction in the RV GLS is a consequence of the adjacency of the right to the left ventricle, which is termed "LV/RV interdependence". Another explanation for the occurrence of LV contractile dysfunction is "the myocardial factor" (3, 26). According to Bilen et al. (3), the mitral valve is integrated with other structures of the left ventricle and the endocardium converges over the mitral valve apparatus, resulting in fibrotic scarring and shortening of this structure together with shortening of the LV longitudinal axis and spherical remodeling of the LV cavity. This so-called "myocardial factor" can depress the LV function independently of the severity of MS (3). This finding was not in agreement with the findings of the present investigation. In this study, the LV strain, strain rate, twist angle, torsion, and rotation were all significantly worsened commensurately with the severity of MS. The LV GLS and GCS, but not the LV twist and torsion, were significantly lower in the MS group than in the healthy individuals. Nonetheless, these significant abnormal values were obvious in the subgroup of patients with mild MS compared to the very severe MS subgroup. The patients with very severe MS also had lower values compared to the severe MS subgroup, but the difference was not significant. Hence, although the rheumatic process can alter myocardial function, which is detected as a reduction in GLS, a decline in preload can worsen the other parameters of contractility such as twist and torsion in any degree of MS severity.

5.1. Limitations

Although 2D strain echocardiography is a simple noninvasive technique for the quantification of the LV rotation, twist, and torsion, it has the intrinsic limitation of the loss of speckles due to the motion outside the imaging plane, resulting in suboptimal reproducibility (27). The thicker sector of 3D strain echocardiography

allows speckles to be captured in larger numbers, in different directions, and at lower frame rates, which can confer a more accurate assessment of cardiac mechanics (1). Nevertheless, the results are varied due to the limited spatiotemporal resolution of 3D echocardiography systems, which are not able to capture events in the fast phases of cardiac cycles (1, 28). However, recent years have witnessed an increase in the use of strain echocardiography and 3D echocardiography. In the current study, 2D was employed in lieu of 3D strain echocardiography to assess myocardial functional parameters. Another study limitation was the lack of standardization of speckle-tracking algorithms among vendors, precluding the definition of an appropriate cutoff value for the LV strain (29).

5.2. Conclusions

The rheumatic process led to a lower ventricular function, which was detectable through the measurement of the LV GLS, GLsr, and GCsr, but not GCS, twist, rotation, and torsional parameters. As the severity of MS progressed, other indices of the LV function such as rotation, twist, and torsion decreased significantly, which showed that theses parameters were more affected by the loading condition than by the rheumatic process per se.

5.3. Ethical Approval

IR.RHC.REC.1399.127

5.4. Informed Consent

Written informed consent was obtained from all patients and the study was approved by the local Ethic Committee of the institute.

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Authors' Contribution

1. Study concept and design: A.A. and A.M. 2. Acquisition of data: A.A. and A.M. 3. Analysis and interpretation of data: A.A. and A.M. 4. Drafting of the manuscript: A.A. and A.M. 5. Critical revision of the manuscript for important intellectual content: A.A. and A.M. 6. Statistical analysis: R.A. 7. Administrative, technical, and material support: A.A. and A.M. 8. Study supervision: A.A. and A.M.

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