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Assessment of Left Ventricular Function in Patients Complicated with Rheumatic Mitral Stenosis using Strain/Strain Rate Trans-Thoracic Echocardiography

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ABSTRACT

Background: Rheumatic valvular heart disease may affect the left ventricular function due to either inflammatory involvement and/or associated hemodynamic disturbance. Rheumatic mitral valve stenosis doesn't affect LV function at early stages but, in the late stage, untreated significant mitral stenosis clinical left ventricular dysfunction may be observed. Patients with mitral stenosis have been observed to exhibit ultrastructural abnormalities in LV muscle cells. Strain and strain rate echocardiography are imaging modalities that may help to diagnose subclinical dysfunction of multiple cardiac chambers. SR/SRE were selected over tissue Doppler velocities because they are not impacted by push-pull forces. Preload and heart rate influence SE, but neither factor affects SRE. Utilizing strain/strain rate imaging, the left ventricular function of participants with rheumatic mitral stenosis was evaluated.

Methods: This was a comparative (case-control) prospective study. 57 subjects were included in the study. The study comprised two groups. There were 32 patients with isolated severe mitral valve stenosis and 25 control cases, all of whom had little or no symptoms (NYHA classes I or II).

Results: The LA, RA, and RV values were significantly lower in cases compared to controls when examining the general features of patients with mitral stenosis and healthy controls. When compared to controls, peak systolic strain was substantially lower in patients. Compared to controls, patients had considerably lower peak systolic strain rates.

Conclusion: Even though the individuals with mitral stenosis had a normal global ejection fraction and no overt signs of heart failure, an echocardiogram indicated LV dysfunction. In the early phases of mitral stenosis, novel echocardiographic techniques like strain/strain rate imaging and TDI may be helpful for evaluating LV function.

Keywords: *Left Ventricle, Strain/Strain Imaging, Mitral Stenosis, Rheumatic.*

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1. INTRODUCTION

Rheumatic heart disease (RHD) is one of the common preventable causes of cardiovascular morbidity and mortality among young populations, despite that RHD burden has declined worldwide, it is still prevalent in some regions especially sub-Saharan Africa, south Asia and generally in overcrowded with mid and low socio-economic countries (1, 2).

The mitral valve (MV) affection in the form of mitral regurgitation is common, especially in the early stage, while mitral stenosis usually develops later, primarily due to persistent or recurrent valvulitis (3&4).

Despite substantial discussion and study of the hemodynamic and clinical influences of RHD with significant valvular involvement, there is still debate about the frequency and relevance of impaired left ventricular (LV) myocardial function in patients with rheumatic mitral stenosis. When all other parameters are held constant, decreased LV myocardial

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function or mechanical blockage caused by the stenotic valve may cause circulatory dysfunction in rheumatic mitral stenosis (5).

Transthoracic echocardiography (TTE) combined with different Doppler modalities (Color, continuous, pulsed wave Doppler) is the primary imaging modality for the screening, diagnosis, and follow-up of patients with RHD.

Diagnostic tests used to assess different cardiac structures and functions have limitations, so combining different imaging modalities may help to minimize the effect of limitations on diagnostic accuracy and management of different cardiac diseases (6).

Due to inflammatory and hemodynamic causes, rheumatic MS compromises LV function on several levels. In rare cases of MS, LV systolic function is often maintained in excellent condition. A small percentage of individuals with MS may have pathogenic, ultrastructural alterations in their LV muscle cells (6).

Patients with mitral valve stenosis display subclinical systolic dysfunction, according to tissue Doppler imaging (TDI). The evaluation of regional heart functions using TDI velocity analysis has shown several issues, including the continuing development of structures resembling the myocardium and the transmission of active and passive deformation to neighboring segments. Furthermore, the heart is quite a distance from the transducer owing to respiration, which has varying velocities (7).

To address these issues, strain echocardiography (SE) and strain rate echocardiogram (SRE) were developed. Tissue Doppler velocities have been demonstrated to be less exact than SE and SRE techniques because of the push-pull forces between neighboring segments. SRE shows parallelism to inotropic circumstances and contractility independent of the loading conditions, while SE is affected by preload and heart rate (8).

Recent studies have shown that individuals with pure mitral stenosis and normal left ventricular function have subclinical LV dysfunction, which is shown by those imaging modalities (9).

We thought to investigate the subclinical changes in LV function in patients rheumatic mitral stenosis using strain/strain rate imaging.

2. MATERIAL AND METHODS

This is a prospective study done in two centres in Cairo, Egypt. (Islamic Center of Cardiology Al-Azhar University and Cardiology Department of Al-Hussien University Hospital) between March 2020 and August 2022.

Patients were divided into patient and control groups. With individuals assigned to patients group were selected according to the following inclusion criteria

1. Patients diagnosed to have isolated moderate or severe MS as assessed by the standard TTE according to the guidelines recommendations(10,11&12).
2. Asymptomatic patients who are free from symptoms related to MS.
3. Patients provided informed consent to participate in the study.

The other control group inclusion criteria were.

1. Completely healthy volunteers without any cardiac or valvular abnormality or symptoms.

The exclusion criteria for the study were.

1. Patient’s refusal to participate in the study.
2. Patients with moderate-to-severe aortic and mitral regurgitation, aortic stenosis.
3. Severely calcified mitral valve structure.
4. Impaired LV systolic function.
5. LV segmental wall motion.
6. Symptomatic patients with NYHA class III or IV.
7. Patients suffering heart failure symptoms.
8. Atrial fibrillation or any significant rhythm irregularity.
9. Patients with diabetes mellitus.
10. Patients with hypertension.
11. Patients with associated significant coronary artery disease.
12. Hyperthyroidism.
13. Chronic obstructive pulmonary disease.

Echocardiography

The standard TTE scan was performed according to the recommended guidelines using a GE Vingmed (Vivid E95) (GE Healthcare, USA) ultrasound system and a 2.5 MHz transducer. An ECG-triggered scan was performed on all patients.

MVA was measured using the two-dimensional (2D) pictures obtained from the parasternal short axis were utilized to calculate planimetrically and using the pressure half-time approach.

By arithmetically averaging the two distance measurements, we were able to calculate the entire area. Valvular insufficiency severity was assessed using both continuous and colour Doppler echocardiography. Teichholz and modified Simpson's methods were used to determine (LV EF).

On apical four-chamber images, TDI was used to evaluate systolic (Sm), early (Em), and late diastolic (LD) velocities in the basal lateral segment and basal interventricular septum (Am)(11&13).

SE/SRE Imaging

After the echocardiographic data was independently collected by two different cardiologists, the mean value of the two measurements was determined. To begin with, the wall perpendicular to the transducer was chosen for the data from the tissue velocity imaging (TVI) tool's 2D imaging.

The LV lateral, septal, anterior, and inferior walls were imaged using colour Doppler myocardial technology with a frame rate of >120/s in the apical two and four chamber views.

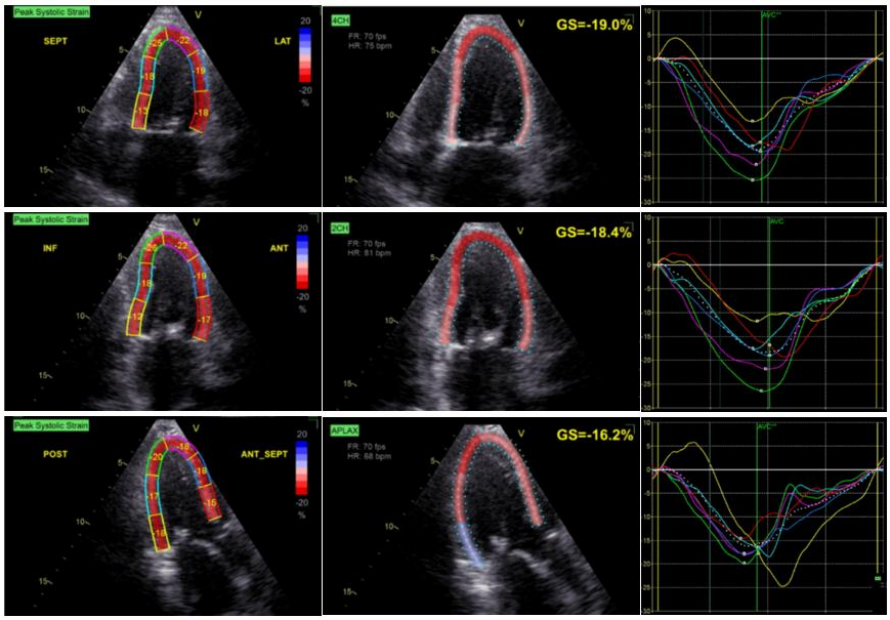

Figure 1: The GE Workstation (EchoPac, GE Healthcare, USA) was used to analyze these color Doppler cardiac pictures in the offline mode. Additionally, measurements of peak systolic strain rate (PSSR) and peak systolic strain (PSS) were taken from the basal, middle, and apical regions of each wall. A 10 mm gap was left between the two sites since measurements were taken just underneath the endocardium. No matter whether they were in the sick or control groups, each person's twelve segments were examined. The study disregarded any segments with unclear images or angle gradients higher than 25°.

Ethical Approval

Following approval of the experiment by the local ethical committee in each center, each participant in the study supplied written informed consent, which was collected. This study's execution was performed according to the Declaration of Helsinki, the World Medical Association's rule of ethics for human subjects research.

Statistical Analysis

IBM SPSS version 22.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp) was used for the analysis. Continuous variables are presented as mean and standard deviation or median and interquartile range according to the distribution of the data after performing Kolmogorov-Smirnov normality tests. Categorical variables are presented as numbers and frequency. The median was utilized in nonparametric analysis and the interquartile range in parametric analysis. We used the (0.05) significance threshold to establish the significance of the findings. The Chi-Square test is used to compare two or more groups. The Monte Carlo test may be used to adjust for any number of cells with a count less than 5. Fischer Chi-Square adjustment was applied to tables demonstrating non-continuous data.

3. RESULTS

This Study includes 57 subjects. There were 25 healthy subjects (control) and 32 patients.

43 (75.4%) were females, 24 (75%) in the patients group and 19 (76%) in the control group, the mean age was 39.08 ± 7.96 years for the patients group and 38.23 ± 6.02 years for the control group (p=0.6) (Table 1).

The mean MVA was 1.4±0.3 cm^2 for the patient group, LV EF% measured by Simpsons method 62.6±4.6% for the patient group and 64.8 ± 4.3% for the control group (p=0.060), the rest of all echocardiographic assessment are summarized in Table 1.

Table (1): General characteristics of mitral stenosis patients and healthy people

Variables	Cases (N = 32)	Control (N = 25)	P. Value
Gender, Male Female	 8 (25%) 24 (75%)	 6 (24%) 19 (76%)	 0.93
Age, years	39.1 ± 7.9	38.2 ± 6.0	0.65
Body Mass Index, kg/m^2	27.2 ± 3.4	26.5 ± 3.0	0.37
Mitral , cm^2	1.4 ± 0.3	-	-
LVDD, mm	45.7 ± 5.1	43.9 ± 4.1	0.16
LVSD, mm	30.6 ± 3.5	30.2 ± 3.6	0.67
IVS, mm	8.3 ± 1.1	8.9 ± 1.4	0.05
PW,mm	8.9 ± 1.2	9.1 ± 1.4	0.55
LVEF Teichholz, %	63.6 ± 3.9	65.6 ± 4.4	0.08
LVEF Simpson, %	62.6 ± 4.62	64.8 ± 4.3	0.06
LA,mm	45.9 ± 6.8	32.0 ± 3.5	<0.0001*
RA,mm	37.9 ± 5.08	32.4 ± 2.69	<0.0001*
RV, TM	37.8 ± 5.2	34.5 ± 2.9	0.003*
PASP, mmHg	40.08 ± 17.43	-	-

BMI-body mass index, **IVS**- interventricular septum, **LA**-left atrium, **LVDD**-left ventricle end-diastolic diameter, **LVEF**- left ventricle ejection fraction, **LVSD**- left ventricle end-systolic diameter, **MVA**- mitral valve area, **PASP**-pulmonary artery systolic pressure, **PW**-posterior wall, **RA**- right atrium, **RV**- right ventricle.

* Significant difference.

There are no significant differences between the two groups in terms of LV dimensions, LV EF%, while left atrium (LA) dimensions, right atrium (RA) dimensions, and right ventricle (RV) function show a significant difference p<0.0001, p<<0.0001, and p=0.003 respectively.

Peak systolic strain and strain rate of all LV segments were considerably lower in patients compared with controls (p<0.0001) Table 2, Table 3.

Table (2): Values of peak systolic strain in studied groups

Variables	**Cases (N = 32)**	**Control (N = 25)**	**P. Value**
Basal Lateral	-13.2 ± 1.7	-15.7 ± 1.8	<0.0001*
Mid Lateral	-13.4 ± 1.5	-17.5 ± 1.9	<0.0001*
Apical Lateral	-13.6 ± 1.9	-16.6 ± 1.9	<0.0001*
Basal anterior	-14.0 ± 1.7	-17.5 ± 2.0	<0.0001*

Mid Anterior	-14.1 ± 2.4	-17.7 ± 1.9	<0.0001*
Apical anterior	-14.6 ± 1.9	-17.4 ± 2.1	<0.0001*
Basal septum	-14.6 ± 1.9	-19.6 ± 1.7	<0.0001*
Mid septum	-14.7 ± 2.1	-20.6 ± 1.8	<0.0001*
Apical septum	-16.0 ± 1.7	-20.3 ± 2.1	<0.0001*
Basal inferior	-13.9 ± 1.7	-16.9 ± 1.2	<0.0001*
Mid inferior	-14.3 ± 2.4	-17.4 ± 1.4	<0.0001*
Apical inferior	-15.1 ± 1.3	-17.9 ± 2.1	<0.0001*

* Significant difference

Table (3): Values of peak systolic strain rate in studied groups

Variables	Cases (N = 32)	Control (N = 25)	P. Value
Basal Lateral	-1.2 ± 0.1	-1.5 ± 0.2	<0.0001*
Mid Lateral	-1.2 ± 0.2	-1.5 ± 0.2	<0.0001*
Apical Lateral	-1.3 ± 0.2	-1.5 ± 0.2	<0.0001*
Basal anterior	-1.3 ± 0.1	-1.54 ± 0.15	<0.0001*
Mid Anterior	-1.3 ± 0.1	-1.6 ± 0.1	<0.0001*
Apical anterior	-1.4 ± 0.2	-1.6 ± 0.2	0.0001*
Basal septum	-1.3 ± 0.2	-1.7 ± 0.2	<0.0001*
Mid septum	-1.3 ± 0.2	-1.7 ± 0.1	<0.0001*
Apical septum	-1.3 ± 0.2	-1.7 ± 0.2	<0.0001*
Basal inferior	-1.3 ± 0.2	-1.5 ± 0.2	<0.0001*
Mid inferior	-1.3 ± 0.2	-1.5 ± 0.2	<0.0001*
Apical inferior	-1.4 ± 0.1	-1.6 ± 0.2	0.0001*

* Significant difference

4. DISCUSSION

This is a prospective study in which a group of patients with isolated significant MS (32 patients) compared to a control group of healthy individuals (25 individuals) in terms of assessment of LV function using SE and SR modality, the main findings are despite the non-significant difference between the two groups in the LV function measured by LVEF both Teichholz and Simpson methods (63.6 vs 65.6 ± 4.4, p=0.08) and (62.6 vs 64.8 ± 4.3, p=0.06) respectively, the SE and SR of all LV segment was lower in patients group (p<0.0001).

In patients with isolated MS and normal LV function, conventional echocardiography methods were utilized to identify subclinical LV dysfunction. To diagnose and treat heart disease, patients must undergo a myocardial function test (14). Even after all these years, research is still being done to determine the most accurate way to calculate the myocardial contractile capacity.

Simsek et al. (15) found in a similar study that patients in Group 1 with mitral stenosis had significantly lower systolic myocardial velocity (Sm) than those in Group 2. Acceptable restrictions Furthermore, compared to Group 2, Group 1 showed a considerably decreased early diastolic myocardial velocity (Em). However, late diastolic myocardial velocity did not vary significantly across the groups (Am). Peak systolic strain in Group 1 was lower, and septal wall strain rates in Group 1 were lower than in Group 2. Comparing Group 1 with Group 2, Group 1 had a much lower lateral wall strain rate. Peak systolic strain experienced the same thing(15).

According to a study by Bitan et al. (16) the severity of the stenosis has not altered significantly over a period of 2.38

years in 75 participants (or 88%). Along with defining stenosis in adult rheumatic MS patients, the research also looked for warning signs of stenosis growth and attempted to estimate the incidence of problems. The mean valvular pressure gradient and the area of the mitral valve were significantly different between the two groups, according to the findings of the most recent echocardiographic test (16).

Separate research by Gordon et al. (17) revealed that the mortality rate after 10 years was greater (70%) and that 86% of patients with mitral stenosis were asymptomatic at the time of diagnosis. Patients with mitral stenosis who participated in this research had an average age of 42. In this study, the average age was 39 years. The findings of the second study were more precisely stated. Congestive cardiac failure wasn't present in any of the subjects. Early discovery was crucial given the high death rates, regardless of whether patients were asymptomatic at the time of diagnosis. To evaluate left ventricular function, M-mode, 2-dimensional, and Doppler echocardiography techniques may be utilized (17).

Each doctor evaluates the efficacy of these techniques in their own unique way. This shows that the global ejection fraction may be considered as being within normal limits until the mitral stenosis reaches its most severe state. Participants in the study who had asymptomatic mitral stenosis and normal conventional echocardiogram findings had their systolic function evaluated. Some individuals with mitral stenosis have lower LV ejection fraction.

Chronically low preload and high afterload, a decline in LV compliance caused by IVS movement to the left caused by the rapid filling of the RV, and regional hypokinesia caused by scarred mitral valve expansion over the posterior-basal myocardium are all likely contributing factors to this multifactorial physiopathology (18). According to EF, the patients in our study had total LV functions that were within normal ranges. It was not discovered that segmental wall motion was abnormal.

Despite the PASP being a little bit higher in the PASP group, the right cardiac dilatation was comparable between the two groups. However, in both SE and SRE, the LV systolic function had dramatically declined. According to previous research, percutaneous mitral valvuloplasty significantly enhanced tissue Doppler velocities in most patients with mitral stenosis and LV dysfunction. It was shown that the main causes of this improvement were the MVA and hemodynamic variables. The LVEF didn't go up (9).

The LV myocardium is impacted at various phases of the rheumatic inflammatory process. In a separate study, ultrastructural pathological abnormalities were found within the heart cells of people with mitral stenosis using electron microscopy. Additionally, myofibrils and other cellular components showed these alterations as well. This finding held true across all patients analyzed, regardless of the severity of left ventricular contractile failure. Those with subpar left ventricular ejection lost more myofibrils than those with satisfactory ejection fractions (19).

The most probable cause of the persistently poor ejection performance, despite improvements in preload and afterload after mitral valvuloplasty, is this rheumatic disease. All these modifications point to an inflammatory rheumatic process rather than hemodynamic issues as the cause of the reduced LV myocardial function in individuals with mitral stenosis (20).

Ozdemir et al. (21) found that global and regional L2D strain and strain rates were much lower in patients with pure MS, even though patients with pure MS often had greater LV function as shown by the ejection fraction. The patients' LV systolic dysfunction may be the cause of this.

5. CONCLUSION

Rheumatic heart disease complicated with MS might affect LV function and performance. According to our research, individuals with isolated mitral stenosis had subclinical LV dysfunction even if their LV EF by traditional echocardiographic assessment was within acceptable ranges. SE and SRE may be used as accurate indicators of LV systolic function in individuals who are asymptomatic or hardly symptomatic and exhibit no indications of heart failure. SE/SRE may also be helpful to assess the patient's response at the beginning of the treatment and throughout time in addition to the decision of intervention.

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