Original Article

Assessment of Left Atrial Strain in Patients with Rheumatic Mitral Valve Disease: A Case-Control Study

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Abstract

Background: This study aims to assess left atrial strain attributes in various mitral valve diseases and to clearly distinguish among patients having mitral valve disease with rheumatic carditis or mitral valve prolapse as its etiology, and individuals with normal cardiac structure and function.

Results:43 patients who were suffering from mitral valve disease (Age: 48.23 ± 13.05), including 29 stenotic, 10 regurgitant, and 4 combined (mitral stenosis and mitral regurgitation)and 43 age and gender-matched controls (49.67 ± 12.60) were enrolled in the study. 2D-speckle tracking echocardiography was used to derive LA strain, Conventional echocardiographic modalities Doppler derived variables. Atrial dimensions were found to be increased (LA AP= 43.17 ± 5.77, LA IS= 60.14 ± 5.54). Trans-mitral velocity (2.10±0.56) and pressure gradients (PPG=19.44 ± 8.06, MPG= 10.00 (6.00,14.00)) were significantly higher in the case group. Left atrial volumetric functions such as passive and active emptying fractionswere significantly decreased in patients with rheumatic mitral valve disease (23.00 (15.00, 33.00), 27.00 (12.00, 36.00). Strain analysis displayed compromised left atrial function in cases. ($PALS_{Avg}$: 18.64 ± 7.83, $PACS_{Avg}$: 7.13 ± 3.25)

Conclusions: Strain and strain rate analysis obtained from speckle tracking echocardiography paved the way for the accurate description of left atrial myocardial deformation, and the extent of remodeling in rheumatic MS and MR against healthy controls. LA's reservoir function was altered in addition to atrial contracting strain and emptying fraction. The peak atrial longitudinal strain and left atrial expansion index were revealed to be more affected in MS than in MR.

Keywords: Strain,2D-speckle tracking, Mitral stenosis, Mitral regurgitation

Introduction

Rheumatic heart disease causes an auto-immune inflammatory injury to the cardiac valves, causing mitral stenosis and insufficiency.In India, one of the leading causes of morbidity and mortality is rheumatic heart disease[1].A Global Burden Diseases study has stated that India contributes one-third of the global RHD burden in terms of wide-ranging records.[2]

The left atrium plays asignificantpart in cardiac hemodynamics by acting as a reservoir for the pulmonary venous return. It acts as a passive conduit to pass oxygenated blood into the left ventricle. Furthermore, the active LA contraction throughout the final phase of diastole is responsible for 15-30% of the left ventricular stroke volume. The valve pathology influences the left atrial function and can result in deficient structural and functional compliance.[3]

Non-invasive assessment of LA function by echocardiography is fundamentally by volumetric analysis. Recent advances in echocardiographic parameters to evaluate LA have been made by utilizing deformation analysis i.e., strain and strain rate.[4] Strain is defined as the degree of deformation in response to stress.

Rheumatic mitral valvedisease can increase the hemodynamic load to the atrium which might affectthe left atrial reservoir, conduit, and contractile function[3]. In those patients with associated paroxysmal atrial fibrillation, there was anextra impairment of the left atrial function.[5]Studies have shown that patients with severe rheumatic mitral stenosis with additional pulmonary hypertension had adecrease in the leftatrial strain.[6]Our study concluded that the global longitudinal strain was significantly decreased in patients with mitral stenosis and regurgitation.

Limited studies employed LA strain as the principal modality to evaluate the left atrial function in patients with rheumatic mitral valve disease, especially in the Indian population. Hence, this study aims to bridge the gap found in the literature, to effectively analyze the impact of rheumatic mitral valve pathology on left atrial remodeling and deformation by applying strain and strain rate imaging in echocardiography.

Methods

Study design and population

A prospective case-control study design was carried out at the Department of Cardiology, Kasturba Hospital, Manipal after the Institutional Ethics Committee (IEC) approval.

Patients undergoing echocardiographic evaluation for rheumatic mitral valve disease were the cases for the study, and the recorded images were stored to conduct offline analysis using left atrial strain imaging.

Forty-three patients with isolatedrheumatic mitral valve disease who underwent echocardiographic evaluation were taken as cases. Forty-three age and gender-matched healthy individuals who arrived for a routine check-up at the center were controls for the study. Those subjects with co-existing aortic valve disease, left ventricular dysfunction, atrial septal defect, left ventricular hypertrophy, chest wall deformation, severe pulmonary artery hypertension, and irregular rhythm were excluded from the study.

Echocardiographic Examination

Transthoracic echocardiography was carried out with a Vivid 7-echocardiography system (General Electric) using a 2.5 MHz transducer. Overall morphological and functional assessment was done using conventional techniques such as 2D (e.g., chamber dimensions), M-mode, and Doppler echocardiography (e.g., peak valvular velocities and pressure gradients). Recordings were stored as digital cine-loops of a minimum of three cardiac cycles and transferred to an optical disk medium workstation for offline analysis.

Additionally, parameters such as maximum Left atrial volume (Vol_{max}), minimum LA volume (Vol_{min}), and LA volume pre-A wave (Vol_{PreA}) were obtained. This was by measuring the volume just before the mitral valveopening at the mitral valve closure and the onset of the P wave in the Apical four-chamber view respectively.

By the application of these values, volumetric analysis was carried out. The left atrial functions deduced from this are[3]:

$$\text{LA Expansion Index} = ((Vol_{max} - Vol_{min}) / Vol_{min}) \times 100$$

$$\text{LA Passive emptying fraction} = ((Vol_{max} - Vol_{PreA}) / Vol_{max}) \times 100$$

$$\text{LA Active emptying fraction} = ((Vol_{PreA} - Vol_{min}) / Vol_{PreA}) \times 100$$

Speckle Tracking Echocardiography (STE)

This is a technique of tracking the natural acoustic speckles on standard 2-Dimensionalultrasound images distributed throughout the myocardium. These markers are tracked frame to frame, which can aid strain and strain rate calculations.

By means of LA strain imaging the three predominant functions of LA can be assessed. The reservoir function is evaluated by the total strain (ε_s), the conduit function by passive strain (ε_e), and the booster pump function is reflected by the active strain (ε_a).

The endocardial border of the left atrium is traced manually in the standard apical four, two, and three-chamber views, thereby describing the region of interest.

Manual adjustment of the region of interest and segmental tracking quality analysis is performed, at the end of which the longitudinal strain curves are generated for each specific atrial segment.

The Peak Atrial Longitudinal Strain (PALS) and the Peak Atrial Contraction Strain (PACS) were taken. These are acquired at the end of the reservoir phase and just before the start of the active atrial contractile phase respectively.

Statistical Analysis

All data were entered in an Excel spreadsheet and analyzed using an independent sample test when the variables were normally distributed. The Mann Whitney U test was applied when the data were skewed to compare the median between the groups, and the Chi-square test wherever applicable. Continuous variables were expressed at Mean ± SD whereas categorical variables were expressed as percentages. Microsoft Excel and SPSS were the preferred softwareused for the analysis and a P value <0.05 was considered statistically significant.

Ethical Approval

This study was conducted following approval from the Institutional Ethics Committee (IEC), Kasturba Hospital, Manipal, Manipal Academy of Higher Education under the approval number IEC-861/2017 on December 13th, 2017.Before participatingin the study, informed consent was taken from the patient.

Results

This study included 29 patients with mitral stenosis, 10 with mitral regurgitation, and 4 with co-existing MS and MR. Among the forty-three patients with isolated rheumatic mitral valve disease who participated in the study, 19 were males (44.1%) and 24 were females (55.8%),

Parameters	Mean +/- SD	P value

along with forty-three age and gender-matched healthy controls. The age distribution was alike in both groups, with the mean value being 48.23 ± 13.05 in rheumatic mitral valve disease patients and 49.67 ± 12.60 in controls. The p-value was 0.592 for the sameand other baseline demographic and clinical characteristics are mentioned in **(Table 1).**

Conventional echocardiographic evaluation between cases and controls clarified that there is no significant difference in the LV systolic function among the selected two groups.

However, the left and right atrium manifested a significant increase in dimensions, with the P value being <0.001.

Doppler findings of the cardiac valves elucidated that the peak velocities of the mitral and tricuspid valves along with their pressure gradients were significantly increased in cases, owing to the hemodynamically expected changes of the valve function, and the P value was found to be <0.001.

Table 1. Echocardiographic parameters by 2-dimensional and Doppler techniques: Comparison between cases and controls

		Rheumatic Mitral Valve Disease (43)	Controls (43)	
EDD (mm)		46.91 ± 6.19	45.84 ± 4.68	0.455
ESD (mm)		28.98 ± 4.44	28.79 ± 3.44	0.892
EF (%)		68.09 ± 4.59	67.23 ± 3.79	0.288
FS (%)		38.02 ± 3.69	37.28 ± 3.17	0.251
Septum thickness (mm)		9.33 ± 1.44	9.70 ± 1.50	0.363
Posterior Wall thickness (mm)		8.86 ± 1.32	9.26 ± 1.38	0.346
Aorta Root (mm)		27.56 ± 4.01	28.95 ± 2.95	0.036
LA(AP)(mm)		43.17 ± 5.77	32.56 ± 3.17	***<0.001***
MACS (mm)		17.58 ± 1.91	17.79 ± 1.30	0.210
LA(IS)(mm)		60.14 ± 5.54	43.47 ± 4.08	***<0.001***
RA(IS)(mm)		50.51 ± 5.12	44.35 ± 3.99	***<0.001***
MPA (mm)		22.53 ± 1.07	22.91 ± 1.13	0.053
Mitral Valve	P.V(m/s)	2.10±0.56	0.80±0.10	***<0.001***
	PPG (mmHg)	19.44± 8.06	2.80±0.86	***<0.001***
	MPG (mmHg)	10.00(6.00,14.00)	1.2 (0.8,1.3)	***<0.001***
Tricuspid Valve	P.V(m/s)	0.64±0.11	0.56±0.07	***<0.001***
	PPG (mmHg)	1.92±0.83	1.31±0.45	***<0.001***
	MPG (mmHg)	1.0 (0.5,1.3)	0.60 (0.50, 0.90)	0.007
Aortic Valve	P.V(m/s)	1.21±0.34	1.19±0.24	0.725
	PPG (mmHg)	5.70 (4.00, 8.00)	5.70 (4.00, 7.80)	0.411
	MPG (mmHg)	3.00 (2.00, 4.00)	2.6 (2.0, 4.0)	0.474
Pulmonary	PV(m/s)	0.81±0.14	0.81±.127	0.937

Valve	PPG (mmHg)	2.95±1.04	2.858±1.00	0.597
	MPG (mmHg)	1.60±0.563	1.45± 0.59	0.099

Abbreviations: EDD: End Diastolic Dimension; ESD: End Systolic Dimension; EF: Ejection fraction; FS: Fractional Shortening; LA(AP): Left atrium (Anteroposterior);MACS: Maximum Aortic Cusp separation; LA(IS):Left Atrium (Inferosuperior); MPA: Main Pulmonary Artery; PV: Peak Velocity; PPG: Peak Pressure Gradient; MPG: Mean Pressure Gradient

Table 2. exhibits the results of left atrial function derived from manually obtained LA volumes and deformation analysis by speckle tracking echocardiography. There was a marked reduction in left atrial function compared to the controls, with a P value of <0.001. Left atrial wall segments from standard apical 2,3 and 4 chamber views were analyzed using 2D speckle-tracking echocardiography to obtain LA strain parameters (**figure 1**) such as PALS and PACS which demonstrated significantly lower values in patients with rheumatic mitral valve disease and the P value was <0.001.

Figure 01: 2D speckle tracking echocardiography revealing LA strain

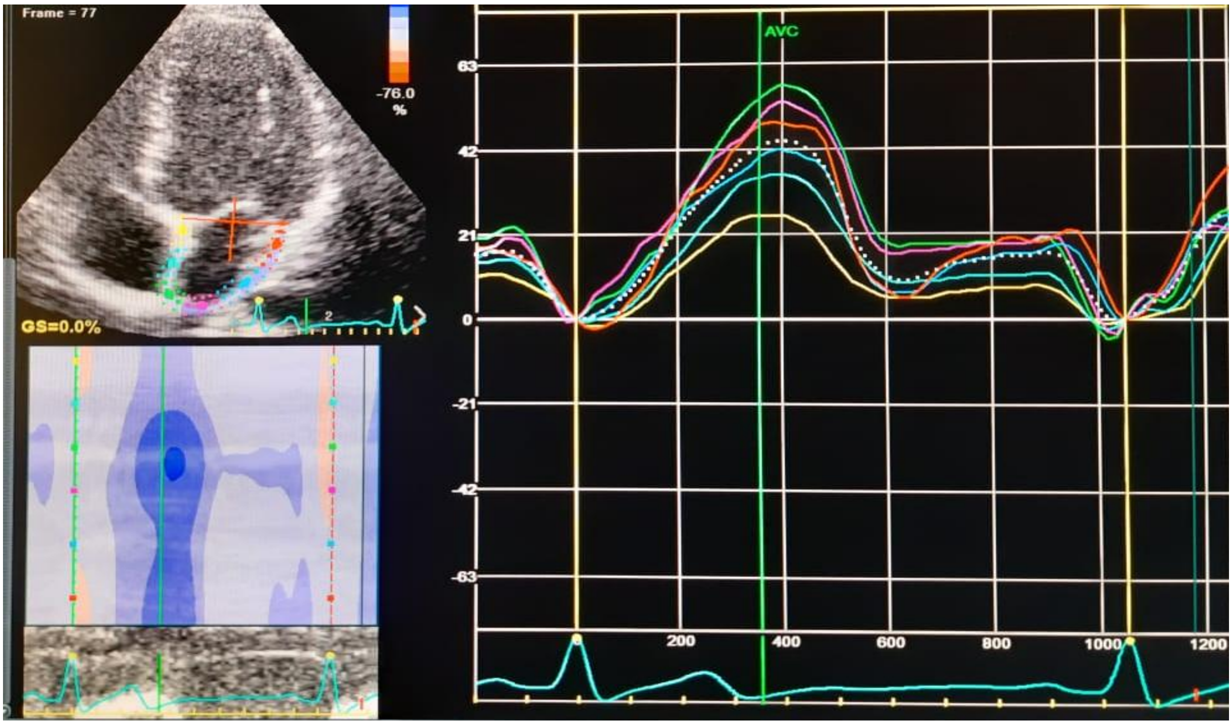

Table 2. Left atrial function by Volumetric analysis and Speckle tracking echocardiography.

	Parameters n=43	Mean±SD/Median (IQR)		Pvalue
		Rheumatic mitral valve disease (43)	Control (43)	
Volumetric Analysis	LA Passive Emptying Fraction (%)	23.00 (15.00, 33.00)	44 (39, 48)	<0.001
	LA Active Emptying Fraction (%)	27.00 (12.00, 36.00)	43 (39, 46)	<0.001
	LA Expansion Index	42.00 (31.00, 72.00)	220 (196, 238)	<0.001

Speckle Tracking Echocardiography	PALS (%)	4CH view	18.19(14.69,23.16)	30.31 (24.5, 40.03)	***<0.001***
		3CH view	17.50±7.93	28.75±11.30	***<0.001***
		2CH view	18.96±9.41	29.19±8.99	***<0.001***
		Average	18.64 ±7.83	30.32±8.84	***<0.001***
	PACS (%)	4 CHview	6.88(3.75, 9.25)	13.41(10.25,17.34)	***<0.001***
		3CH view	6.25(4.06, 7.88)	10.98 (8.44, 15)	***<0.001***
		2CH view	7.66(3.75, 10.50)	11.81 (10, 15.47)	***<0.001***
		Average	7.13±3.25	13.00±4.19	***<0.001***

Abbreviations:PALS: Peak Atrial Longitudinal Strain; PACS: Peak Atrial Contraction Strain.

Additionally, LA function parameters were compared between MS and MR. Resultant volumetric values depicted a higher alteration i.e., an increased volume in the regurgitant lesion whereas the strain analysis revealed that stenotic mitral valve produces a gross reduction in left atrial function. Therefore, it is inferred that pressure overload conditions such as MS have a more consequential role in LA deformation than a volume overload burden to LA in MR, regardless of being statistically insignificant. This could be due to the smaller sample size of isolated MS and MR taken for this study. Patients with MS had a distinctly lower PALS and LA expansion index than those with MR as illustrated in **Table 3.**

Table 3. Left atrial function: Comparison between MS and MR

Parameters (n=39)	Median (IQR)		Pvalue
	MS (n= 29)	MR (n=10)	
LAPassiveEF (%)	21(13.5-33)	28(17.75-30.75)	0.22
LAActiveEF (%)	26(13.5-35.5)	28.5(25.93-16.83)	0.41
LA Expansion index	35(31-55)	88.5(41.75-122.5)	0.004*
PALS4C (%)	16.25(13.21-21.02)	21.06(14.84-32.26)	0.11
ACS4C (%)	6.38(3.60-9.74)	8(5.32-8.77)	0.83
PALS3C (%)	14.22(11.25-20.61)	17.81(14.17-25.18)	0.13
ACS3C (%)	5.78(3.36-7.54)	6.48(4.55-9.44)	0.34
PALS2C (%)	14.53(10.55-22.26)	21.41(17.54-29.48)	0.02*
ACS2C (%)	6.34(2.85-9.74)	9.82(6.89-11.0)	0.12
PALS average (%)	15.29(11.54-20.74)	21.67(16.11-31.0)	0.03*
ACSaverage (%)	6.38(3.85-8.96)	8.61(5.93-9.40)	0.11

Abbreviations:LA: Left atrium; EF: Ejection Fraction; PALS: Peak Atrial Longitudinal Strain; ACS: Atrial Contraction Strain

Discussion

Mitral valve disease plays a pivotal role in limiting normal cardiac hemodynamics. Mitral regurgitation, especially in a chronic setting,produces apparent left atrial remodeling and dysfunction. The key observations gathered from this study wereconsistent with that patients with mitral valve disease, because of rheumatic pathology, bring about evident changes in left atrial function.[7-9] The dimensions of the left and right atrium and pulmonary artery were significantly increased along with the elevation of pulmonary artery pressures. This chamber enlargement was not reflected in the left ventricle since most of the cases enrolled in the study had mitral stenosis, which as it is, does not contribute to left ventricular dysfunction. By employing standard volumetric assessments, the left atrial passive and active emptying fraction showed a notable reduction in its values. In addition, the LA expansion index was also found to have decreased. Considerable difference in LA expansion index was noted when patients with mitral stenosis were compared to those with mitral regurgitation, with results revealing stenotic lesions to have a more pronounced negative impact on LA deformation. Among the strain interpretations that demonstrated a marked reduction in their values in patients with mitral valve disease were the average left atrial PALS and the average left atrial PACS in contrast to the values obtained from normal individuals. This finding was exhibited in all routine echocardiographic views.Furthermore, peak velocities, peak pressure gradients, and the mean pressure gradients across the mitral and tricuspid valve were considerably elevated in patients.

Kono, et al. in 1992, USA hypothesized that increased pressure in the LA myocardium can result in gradual intrinsic left atrial dysfunction.[10] Conventional methods were found to be inefficient in tracking the myocardial segments accurately[17,18] and therefore SRI was proved to be applicable in this scenario for a precise estimation by our study.

P. Caso, et al from Italy in the year 2019, demonstrated that atrial myocardial deformation characteristics were abnormal in asymptomatic patients with moderate MS and that strain rate imaging could detect early LA reservoir dysfunction in such patients.[11]LA remodeling was deduced to be the main consequence of mitral stenosis with strikingly decreased PALS values in severe stages of MS by Shojaeifard M, et al in 2020.[14]The significantly reduced PALS measurements from our study were consistent with this finding.

A study conducted by Ranien H. El-Shafai, et al. in Egypt,2019 including 22 patients with MS, 14 patients with mitral regurgitation, and 14 with both MS and MR concluded that LA function was significantly reduced in combined MS and MR lesions based on LA indices such as LA emptying fraction, LA passive emptying fraction, atrial fraction, and LA expansion index among groups, which served to be supporting evidence.[12]However the variation in the extent of dysfunction in LA between the two isolated lesions was not documented. This was successfully explained with the conclusive findings from our study showing pressure overload and resistance to LA ejection in MS precipitated predominantly higher LA deformation than MR.

Atrial fibrillation is a prevalent arrhythmia associated with nearly 29% of patients with isolated mitral stenosis and in 16% with isolated mitral regurgitation [5,15], the exclusion of which leaves out a promising scope in further understanding the LA myocardial changes assessed using strain since the methodology used for the same requires regularity in the cardiac rhythm.

Further studies can be steered in the direction of clinical outcomes and prognostic aspectsabout long-term follow-up and indications for intervention in asymptomatic mitral valve diseases with the functional results from this analysis as reference.

Limitations of the study

The small sample size is one of the main limitations of this study. Though there were normal subjects who were controls, comparing patients with MS and MR would have been more accurate if the sample size had been larger. Another limitation is that patients with atrial fibrillation were excluded. However, the methodology used for measuring the strain parameters requires a regular rhythm.

Clinical implications

Despite our study not including the prognostic implications, similar studies have shown that poor long-term prognosis and additional impairment of the left atrial function were linked to mitral valve pathology.[11,16.]

Conclusions:

Speckle-tracking echocardiography-derived strain and strain rate analysis paved the way for the accurate description of left atrial myocardial deformation, the extent of remodeling in rheumatic mitral stenosis and regurgitation against healthy controls, as well as a contrasting evaluation of the degree of LA dysfunction between MS and MR. LA's reservoir function was altered in addition to atrial contracting strain and emptying fraction. The peak atrial longitudinal strain and left atrial expansion index were revealed to be more affected in MS than in MR.

List of abbreviations:

MS-Mitral stenosis

MR-Mitral regurgitation

LA-Left Atrium

LV-Left Ventricle

PPG-Peak Pressure Gradient

MPG-Mean Pressure Gradient

PALS-Peak Atrial Longitudinal Strain

PACS- Peak Atrial Contraction Strain

RHD-Rheumatic Heart Disease

STE-Speckle Tracking Echocardiography

SR-Strain Rate

SPSS-Statistical Package for Social Sciences

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