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Research Brief

Left atrial function by two-dimensional speckle tracking echocardiography in patients with severe rheumatic mitral stenosis and pulmonary hypertension

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ABSTRACT

We studied left atrial (LA) function in severe rheumatic mitral stenosis (MS) patients using two-dimensional speckle tracking echocardiography (STE). Eighty patients with isolated severe MS in sinus rhythm and 40 controls underwent comprehensive echocardiography including STE derived LA strain [reservoir strain (LAS_r), conduit strain (LAS_{cd}) and contractile strain (LAS_{ct})]. The mean MVA was 0.93 ± 0.21 cm^2. The mean values of LAS_r ($14.73 \pm 8.59\%$), LAS_{cd} ($-7.61 \pm 4.47\%$) and LAS_{ct} ($-7.16 \pm 5.15\%$) in patients were significantly lower ($p < 0.001$) vs. controls $44.11 \pm 10.44\%$, $-32.45 \pm 7.63\%$, $-11.85 \pm 6.77\%$ respectively and showed decreasing trend with increasing MS severity and higher NYHA class. In conclusion, LA dysfunction is prevalent in severe MS irrespective of NYHA functional class.

1. Introduction

Mitral stenosis (MS) is the most common valve lesion in chronic rheumatic heart disease (RHD) causing obstruction to left ventricular (LV) diastolic filling.[1] The resultant chronic left atrial (LA) pressure overload leads to atrial muscle bundle disorganization and fibrosis resulting in both atrial stiffness and atrial reservoir dysfunction[2] and ultimately leads to development of post-capillary pulmonary hypertension (PH).[3] The LA dysfunction in rheumatic MS can be quantified by deformation imaging i.e. two-dimensional (2D) speckle tracking echocardiography (STE).[4–6] Most previous studies have either assessed global LA strain, reservoir or conduit strain with contractile strain being reported only in mild to moderate MS.[5,6] We aimed to assess LA function (reservoir, conduit strain and contractile strain) by STE and its correlation with NYHA functional class and echocardiography parameters in patients with isolated severe MS with pulmonary hypertension and healthy controls.

2. Methods

This prospective study enrolled 80 patients with isolated severe MS (mitral valve area (MVA) $\leq$1.5 cm^2) in sinus rhythm with pulmonary hypertension (age 18–40 years) and 40 age matched healthy controls. All patients were on optimal medical management. Patients with other significant valve lesions were excluded. The ethics committee approval was obtained and participants provided written informed consent.

The standard 2D, M-mode and Doppler echocardiography was performed (Philips EpiQ-7C) and parameters included LA dimension, LV internal dimension in diastole ($LVID_d$) and systole ($LVID_s$). The LV ejection fraction (LVEF) was calculated by Simpson's method. Peak (PG) and mean diastolic gradient (MG) across the mitral valve was calculated by continuous wave Doppler. Right ventricle systolic pressure (RVSP) was measured from tricuspid regurgitation jet velocity.[3] Three consecutive cardiac cycles were recorded and averaged. PH was graded based on RVSP as mild

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36–45, moderate 46–60 and severe >60 mm Hg.[3] The dyspnea was classified according to the New York Heart Association (NYHA) functional classification.

For left atrial strain measurements, the LA focused four-chamber view was obtained by ECG gated two-dimensional echocardiography.[4] LA strain parameters were derived offline with QLAB 13 software (supplementary Figure 1). A dedicated LA strain measurement software was used. The region of interest (ROI) was selected by delineating the left atrial endocardial contour which was drawn from the mitral annulus on one side with extrapolation across pulmonary veins and LA appendage orifices and ending at the mitral annulus on the opposite side. While drawing ROI, great care was taken that the ROI wraps the LA myocardium only, avoiding the pericardium.

The cardiac cycle was ECG gated and kept from end-diastole to end-diastole with zero reference point being peak of R wave.[4] LA deformation has three phases: a) Reservoir phase: starts at the end of ventricular diastole (mitral valve closure) and continues until mitral valve opening, b) Conduit phase: occurs from the time of mitral valve opening through diastasis until the onset of LA contraction, c) Contraction phase: occurs from the onset of LA contraction until the end of ventricular diastole.[4] The strain values were derived from the strain curves obtained. The peak strain during reservoir phase is reservoir strain (LAS_r), the peak strain during conduit phase is conduit strain (LAS_{cd}) and the peak strain during contraction phase is contractile strain (LAS_{ct}).

Statistical analysis was done with Epi Info 7.1.1 software. Continuous data are presented as mean with standard deviation and compared by *t*-test or ANOVA. Categorical data presented as percentage and compared using a chi-square test. *P* value < 0.05 was considered significant. Analysis of 10 randomly selected subjects was done for inter-observer variability of LA strain by two independent investigators and repeat offline LA strain estimation was done 5 ± 2 days later for intra-observer variability.

3. Results

The mean MVA in patients was 0.93 ± 0.21 cm^2. Severe MS (MVA 1–1.5 cm^2) and very severe MS (MVA <1 cm^2) were present in 44 subjects (55%) and 36 subjects (45%) respectively. The mean RVSP in patients was 60.01 ± 19.88 mm Hg suggesting severe pulmonary hypertension. All three LA strain [reservoir strain (LAS_r), conduit strain (LAS_{cd}) and contractile strain (LAS_{ct})] parameters were significantly reduced in patients vs. controls (p < 0.001) (Table 1). The interclass correlation coefficient for LA strain measurements was 0.95 (95% CI 0.84–0.98) for inter-observer agreement and 0.97 (95% CI 0.94–0.99) for intra-observer agreement, indicating good correlations.

Table 1
Baseline characteristics and echocardiographic parameters among subjects.

	Patients (n = 80)	Controls (n = 40)	*P* value
Age (years)	30.4 ± 6.7	29.5 ± 5.9	0.46
Male: female	1:2.5	1.7:1	–
LA size (cm)	4.67 ± 0.65	2.79 ± 0.41	<0.001
Maximum LA volume (ml)	99.67 ± 34.09	36.07 ± 9.50	<0.001
Minimum LA volume (ml)	64.09 ± 29.61	13.77 ± 4.85	<0.001
LVIDd (cm)	4.40 ± 0.40	4.5 ± 0.21	0.09
LVIDs (cm)	2.79 ± 0.33	2.68 ± 0.18	0.06
LVEF (%)	60.11 ± 2.49	60.57 ± 2.11	0.33
MVA (cm^2)	0.93 ± 0.21	5.17 ± 0.53	<0.0001
PG (mm Hg)	19.33 ± 5.82	–	–
MG (mm Hg)	12.33 ± 4.16	–	–
RVSP (mm Hg)	60.01 ± 19.88	–	–
LAS_r (positive value, %)	14.73 ± 8.59	44.11 ± 10.44	<0.001
LAS_{cd} (negative value, %)	−7.61 ± 4.47	−32.45 ± 7.63	<0.001
LAS_{ct} (negative value, %)	−7.16 ± 5.15	−11.85 ± 6.77	<0.001

LA-left atrium; LVEF- left ventricular ejection fraction; LVIDd-left ventricle internal dimension in diastole; LVIDs-left ventricle internal dimension in systole; LAS_r-left atrium reservoir strain; LAS_{cd}-left atrium conduit strain; LAS_{ct}-left atrium contractile strain; MG-mean diastolic transmitral gradient; MVA-mitral valve area; PG-peak diastolic transmitral gradient; RVSP- right ventricle systolic pressure.

Table 2
Comparison between left atrial strain parameters with various groups based on mean and peak diastolic transmitral gradient, left atrium size, severity of pulmonary hypertension and mitral valve area.

Echocardiography parameters	LA strain values		
	LAS_r (%)	LAS_{cd} (%)	LAS_{ct} (%)
Mean diastolic transmitral gradient (mm Hg)			
<10 (Group I) n = 26	15.06 ± 7.74	−8.54 ± 4.05	−6.77 ± 5.12
10-15 (Group II) n = 32	15.77 ± 7.38	−7.90 ± 4.14	−7.73 ± 4.32
15-20 (Group III) n = 15	13.83 ± 12.32	−6.68 ± 5.76	−7.15 ± 7.18
>20 (Group IV) n = 7	10.77 ± 7.69	−4.80 ± 3.63	−5.87 ± 4.43
Peak diastolic transmitral gradient (mm Hg)			
10-20 (Group I) n = 50	15.20 ± 7.89	−8.12 ± 4.26	−7.13 ± 4.96
20-30 (Group II) n = 25	14.09 ± 10.13	−6.91 ± 4.90	−7.17 ± 5.82
>30 (Group III) n = 5	13.17 ± 8.42	−5.91 ± 4.27	−7.26 ± 4.50
Left atrium size (cm)			
<4 (Group I) n = 11	14.35 ± 7.15	−9.38 ± 4.59	−5.34 ± 3.76
4-5 (Group II) n = 44	15.41 ± 8.17	−7.70 ± 4.22	−7.75 ± 4.94
5-6 (Group III) n = 20	15.10 ± 10.70	−7.31 ± 5.08	−7.56 ± 6.45
>6 (Group IV) n = 5	8.11 ± 2.59	−4.02 ± 1.70	−4.08 ± 2.01
Severity of pulmonary hypertension			
No (Group I) n = 6	19.71 ± 11.67	−9.08 ± 5.06	−10.63 ± 8.03
Mild (Group II) n = 18	15.22 ± 6.67	−8.67 ± 4.44	−6.54 ± 3.16
Moderate (Group III) n = 19	15.37 ± 10.71	−8.01 ± 5.18	−7.28 ± 6.24
Severe (Group IV) n = 37	13.36 ± 7.64	−6.64 ± 3.95	−6.84 ± 4.76
Mitral valve area			
<1 cm^2 (Group I) n = 44	15.60 ± 9.90	−7.87 ± 5.07	−7.80 ± 5.62
1–1.5 cm^2 (Group II) n = 36	13.67 ± 6.63	−7.28 ± 3.65	−6.34 ± 4.47

LAS_r-left atrium reservoir strain; LAS_{cd}-left atrium conduit strain; LAS_{ct}-left atrium contractile strain.

The LA conduit/contractile strain ratio was 1.66 ± 2.15 in severe rheumatic mitral stenosis patients and 4.29 ± 3.81 in controls (*p* < 0.001). However, there was no significant correlation between LA conduit/contractile strain ratio and severity of mitral stenosis. This was likely because of severely impaired conduit strain as well as contractile strain in our patient population of severe mitral stenosis.

Thirty-seven subjects (46.2%) were in NYHA class III, 38 subjects (47.5%) in NYHA class II and 5 subjects (6.3%) in NYHA class I. The MVA was significantly lower in NYHA class III (0.87 ± 0.21 cm^2) vs. NYHA class II (0.97 ± 0.2 cm^2) vs. NYHA class I patients (1.18 ± 0.23 cm^2) [p = 0.004 between all groups] and RVSP was significantly higher in NYHA class III (66.32 ± 19.74 mm Hg) vs. NYHA class II patients (55.03 ± 18.47 mm Hg) [p = 0.01 between class II and III]. Mean LA strain values (reservoir, conduit, contractile strain) were numerically lower in NYHA class III vs. NYHA class I patients but the difference was not statistically significant.

We divided patients into groups based on increasing mean diastolic transmitral gradient (four groups), increasing peak diastolic transmitral gradient (three groups), increasing LA size (four groups), increasing severity of pulmonary hypertension (four groups) and decreasing MVA (two groups) to study their correlation with LA strain (Table 2). The three LA strain parameters showed a non-significant trend towards decline with increasing LA size, decreasing MVA, increasing MG and PG, and increasing severity of PH.

4. Discussion

Our study demonstrates a significant decrease in all three left atrial strain parameters i.e. reservoir, conduit and contractile strain

signifying severe LA dysfunction in patients with severe rheumatic MS. Mahfouz et al[5] reported that in mild MS, LA conduit and reservoir strain were decreased but the contractile strain was well preserved. Another study by Demirkol et al[6] on 52 asymptomatic MS patients with MVA 1.38 ± 0.36 cm^2 and mean diastolic transmitral gradient 7.9 ± 2.8 mm Hg also reported reduced LA reservoir and conduit strain but increased contractile strain. In contrast, our study included only severe MS patients with mean MVA 0.93 ± 0.21 cm^2 and mean transmitral gradient 12.33 ± 4.16 mm Hg. The preserved LA contractile function is a compensatory mechanism to counterbalance reduced LA reservoir and conduit function in mild MS as LV filling predominantly occurs in LA contractile phase in MS in contrast to normal filling pattern where LA filling predominantly occurs in the early conduit phase.[7] Our study shows that LA contractile function is also compromised in addition to reservoir and conduit function in severe MS.

The mean LA size, PG, MG and RVSP was higher with increasing NYHA class while mean MVA was significantly lower in NYHA class III group vs. class II and I group ($p = 0.004$ between all groups). There was a trend towards stepwise decrease in LA reservoir, conduit and contractile strain with deteriorating NYHA class. Our results are different from study by Chien et al[8] on 69 MS patients (84% patients-mild-moderate MS) which showed positive correlation between atrial deformation and NYHA class. The LA strain parameters were markedly decreased in our study making further numerical fall with deteriorating NYHA class inconsequential. Secondly, in their study[8] 57 patients had atrial fibrillation (AF), hence LA contractile strain was not reported. In our study, we excluded AF patients and analyzed all three LA strain parameters. Further, pulmonary hypertension also likely contributed to LA dysfunction as higher pulmonary artery pressures have strong negative correlation with LA compliance.[1,9]

Our study shows that the patients with severe MS regardless of NYHA class develop severe LA dysfunction which worsens with further decline in MVA. Therefore patients with severe MS should be subjected to early and timely balloon mitral valvuloplasty (BMV) as it may improve their LA function.[9,10] Early intervention may also prevent the development of AF, RV dysfunction and improving their prognosis.[11] Finally, many factors could have contributed to LA dysfunction including chronic LA pressure overload, LA fibrosis, adverse remodeling of LA, involvement of mitral apparatus in the rheumatic process, subclinical LV and RV dysfunction.[2,12]

The limitation of our study is inclusion of only isolated severe MS patients as including subjects with regurgitant lesion might have affected the results because of LA volume overload. Also we excluded patients with atrial fibrillation because the STE is ideally for patients with regular heart rhythms as strain values are directly influenced by the length of diastole. We used two-dimensional speckle-tracking echocardiography rather than three-dimensional speckle-tracking echocardiography (3D STE). The 2D speckle tracking is restricted to the assessment of cardiac chamber function in a single plane and may be affected by foreshortened apical views and geometric assumptions. The 3D speckle-tracking echocardiography has the capability for quantitative assessment of LA volumes and strains in 3D space from the 3D acquired datasets. However there are certain issues with 3D STE like dependency on optimal image quality with sufficient frame rate thus requiring dedicated training and skill, lack of cut-offs for differentiating normal versus abnormal values, variability in strain values based on gender and age as well as vendor specific variations in the measured values of 3D strain making it difficult to interpret studies reported on different machines.[13] The above shortcomings of 3D STE need to be addressed before it can be more widely used in research and clinical practice.

5. Conclusion

The present study shows that marked left atrial dysfunction is seen in severe rheumatic MS irrespective of NYHA functional class as revealed by severely reduced left atrial reservoir, conduit and contractile strain. LA function further deteriorated non-significantly with increasing severity of MS suggesting that early and timely intervention in severe MS patients irrespective of NYHA functional class should be undertaken as it may likely improve the LA function. This hypothesis however requires further study.

Declaration of competing interest

All the authors declare that they have no conflicts of interest with respect to the present submission.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2021.12.011.

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