Original Article

Severe Rheumatic Mitral Stenosis, Worse Left Atrial Mechanics is Closely Associated with Echo Criteria for Intervention

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Abstract

Background: Rheumatic mitral valve (MV) stenosis is associated with progressive left atrial (LA) fibrosis and functional impairment, Pulmonary artery systolic pressure (PASP) and right ventricular (RV) dysfunction. The aims of the study were to determine in those patients with severe MV stenosis if LA mechanical function as assessed by speckle tracking echocardiography could identify those with increased PASP, atrial fibrillation (AFib), and RV dysfunction. **Subjects and Methods:** Patients with severe MV stenosis were identified from the institutional echo database. Echocardiograms were read off line and measurements included atrial and ventricular strain. Patients were divided into tertiles of LA reservoir strain (LASr) values and data compared between the groups. **Results:** Ninety-seven patients, 67 females, mean age 47.4 ± 11.9 years, had MV mean gradient of 8.3 ± 5.1 mmHg, MV area by pressure half time of 1.3 ± 0.3 cm^2 and LASr of 11.18% ± 6.4%. Those patients in the lowest LASr tertile had more AFib (72%, $P = 0.0001$), PASP >50 mm Hg (39%, $P = 0.005$), and worst RV impairment. In multivariable logistic regression analysis, LASr, age, and mean MV gradient were the independent predictors of AFib and PASP >50 mm Hg. Cutoffs, determined by receiver operating characteristic curve analysis had high specificity for the composite outcome of Afib and PASP >50 mmHg (85% for LASr <7.7%). **Conclusion:** In severe MV stenosis LASr, age and mean MV gradient, are independent predictors of Afib and PASP >50 mmHg. LASr <7.7% has high sensitivity and specificity in identifying those who meet ESC guideline 2017 criteria for valve intervention, suggesting its potentially helpful addendum to the surveillance of patients with MV stenosis.

Keywords: Atrial fibrillation, atrial strain, mitral stenosis, pulmonary hypertension, rheumatic heart disease, valvular heart disease

Introduction

Rheumatic mitral disease affects as many as 18.6 per 1,000 individuals in the developing world and remains an important cause for valve surgery in the developed world. The 2017 European Guideline on valvular heart disease[1] identify class IB criteria for percutaneous intervention or IC for surgical intervention in severe MS to be the following: (i) presence of symptoms, ii) high risk for thromboembolic events, i.e., new onset or paroxysmal atrial fibrillation (AFib), and (iii) when the risk of hemodynamic decompensation is significantly increased, i.e., in the presence of pulmonary artery systolic pressure (PASP) greater than 50 mmHg at rest. Early identification of patients who are at greatest risk for developing AFib and PASP >50 mmHg may potentially benefit from timely anticipatory intervention. It is however well recognized that there is no close correlation between mitral valve (MV) area and PASP and AFib prevalence. Further, gradients across the MV cannot always accurately identify those with severe MS and its hemodynamic consequences.[1] There is therefore a growing interest in left atrial (LA) size and function as potential predictive markers of unfavorable outcomes in MV disease.[2] Current data exist predominantly for MV regurgitation. LA mechanical function in response to MV stenosis mediates the upstream effects of MV stenosis on the pulmonary vascular bed and right ventricular (RV). Indeed, the combination of LA dimension and strain are the strong predictors of LA pressure.[3]

Access this article online

Quick Response Code:

Website: www.jcecho.org

DOI: 10.4103/jcecho.jcecho_80_21

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Submitted: 14-Nov-2021 **Revised:** 05-Jan-2022
Accepted: 27-Jan-2022 **Published:** 20-Apr-2022

How to cite this article: Vriz O, Feras K, Alamri M, Blassy B, Almozel A, Smith M, *et al*. Severe rheumatic mitral stenosis, worse left atrial mechanics is closely associated with echo criteria for intervention. J Cardiovasc Echography 2022;32:38-46.

LA mechanics may therefore represent a pivotal biomarker in tracking advancing MV stenosis and restore SR and recovery from pulmonary hypertension. It is however under evaluated at present.

The aims of the study were to assess characteristics and differences in LA strain in patients with severe isolated rheumatic MV stenosis meeting guidelines criteria for MV intervention, i.e., the presence of AFib, RV dysfunction, and PASP >50 mm Hg, and those that did not.

Subjects and Methods

Study design

Flowchart 1 describes the derivation of the study population. 1020 consecutive patients with a principal diagnosis of moderate (MV area – measured by pressure half time (PHT) and/or planimetric area and gradients across the valve were concordant for the diagnosis of moderate MV stenosis), moderate to severe (when not all the measurements were concordant for moderate or severe MV stenosis) or severe mitral stenosis (when all the measurements were concordant with severe MV stenosis) were retrospectively identified from the King Faisal Specialist Hospital and Research Center (KFSH and RC), Riyadh, Saudi Arabia, echocardiography database from the period 2010–2019. These patients were in part regularly followed by the KFSH and RC, a tertiary hospital, and part of them were referral from local hospitals. The study was approved by the local institutional ethics review board.

One hundred and twenty of these patients had severe isolated MV stenosis, valve area ≤ 1.5 cm^2 and/or mean gradient more than 5 mmHg,[4] were retrospectively identified from the KFSHRC, Riyadh Saudi Arabia, echo database. The study was approved by the local institutional ethics review board. LA strain analysis was possible in 97 of the 120 (M/F 30/67) patients, and they form the basis of this study. Patients with more than mild concomitant mitral regurgitation or more than mild aortic stenosis and or regurgitation were excluded.

Anthropometric data (gender, age, height, weight, body surface area [BSA]), hemodynamic parameters (blood pressure, heart rate), sinus rhythm or AFib were abstracted from the echocardiographic report.

Echocardiogram

A standardized transthoracic echocardiographic examination under continuous EKG recording was performed according to the American Society of Echocardiography.[5] All studies were reviewed and analyzed offline with an image processing workstation Excelera and on Image Arena version 4.6 software (TomTec Imaging Systems, Unterschleissheim, Germany) for strain analysis.

Two-dimensional measurements of the left ventricle (LV end-diastolic and end-systolic diameters, interventricular septal, and posterior wall thickness) were obtained from the parasternal long-axis view, with the patient in the left lateral position. LV mass was calculated according to the Penn convention.[6] Relative wall thickness was calculated as 2 x posterior wall thickness/LV diameter in diastole. LV ejection fraction (LVEF) was calculated in the apical 4CH and 2CH view using the method of discs. LA volume (LAV) was measured from the apical 4CH and 2CH view according to the American Society of Echocardiography.[5] Pulse tissue Doppler imaging was performed in 4CH view at the septal and lateral mitral annular level. Peak myocardial wave velocity during systole (S`), early diastole (E`), and late diastole (A`) (in centimeters per second) were measured.[6]

Peak and mean mitral gradients were obtained from the apical position using CW Doppler recordings for the estimation of MV stenosis severity. MV area was evaluated using 2D planimetry where possible and the PHT method (220/PHT)[1] [Figures 1 and 2].

Stroke volume (SV) was derived from the formula SV = ($LVOT_{area}$ × LVOT VTI) where LVOT is the left ventricular outflow tract, and VTI is the velocity time integral. LVOT diameter was measured in mid-systole at the aortic annulus level, whereas LVOT VTI spectral Doppler was measured using pulse-wave Doppler. SV then was indexed by BSA. Peak tricuspid regurgitation velocity (TRV) was measured either from any of the following views including the RV inflow of the parasternal long-axis or short-axis views or from the apical 4CH view. The highest velocity across the valve obtained was used for calculating PASP after adding the right atrial pressure estimated, considering the inferior vena cava dimension and collapsibility in inspiration. The grading of tricuspid valve regurgitation (TR) was defined as mild, moderate, and severe [Figure 2].[7] Pulmonary vascular resistance (PVR) was calculated as PVR = TRV/VTI RVOT (cm) x10 + 0.16 where TRV = tricuspid regurgitant velocity, TVI RVOT = time-velocity integral and RVOT = RV outflow tract.[8] Tricuspid annular plain systolic excursion (TAPSE), used to assess the global RV systolic function, was measured from the 4CH by placing an M-mode cursor through the tricuspid annulus measuring the excursion distance between end-diastole and end-systole (in mm) and with optimal image orientation and alignment to avoid underestimation. The longitudinal contraction (S`) and diastolic myocardial velocities (early (E`) and late (A`)) were measured by tissue Doppler imaging at the lateral corner of the tricuspid annulus in 4CH view. Fractional area change (FAC), another parameter of global RV function, was obtained from the 4CH tracing the RV endocardium both in diastole and systole from the annulus to the apex. FAC was defined as (end diastolic area-end systolic area)/end diastolic area × 100.[9]

Left atrial strain

Two-dimensional speckle tracking of the left atrium (LA) endocardial border was traced in the apical 4CH view starting and ending at the level of the lateral and medial points of the mitral annulus, interpolating gaps [Figure 3a]. Tracking results were visually compared to the motion of the underlying atrial

wall (particularly at the mitral ring and the atrial roof) to judge the accuracy of the atrial strain estimation. The atrial strain measurements were made: (a) on the frame just before MV opening, representing the reservoir phase (LA reservoir strain [LASr]) during systole and (b) contracting phase corresponded to the downslope segment of atrial contraction, immediately after the *P* wave (LASct) when the patient was on sinus rhythm. Zero strain reference was set at left ventricular end-diastole. Endocardial tracking was considered[2,10,11] [Figure 4].

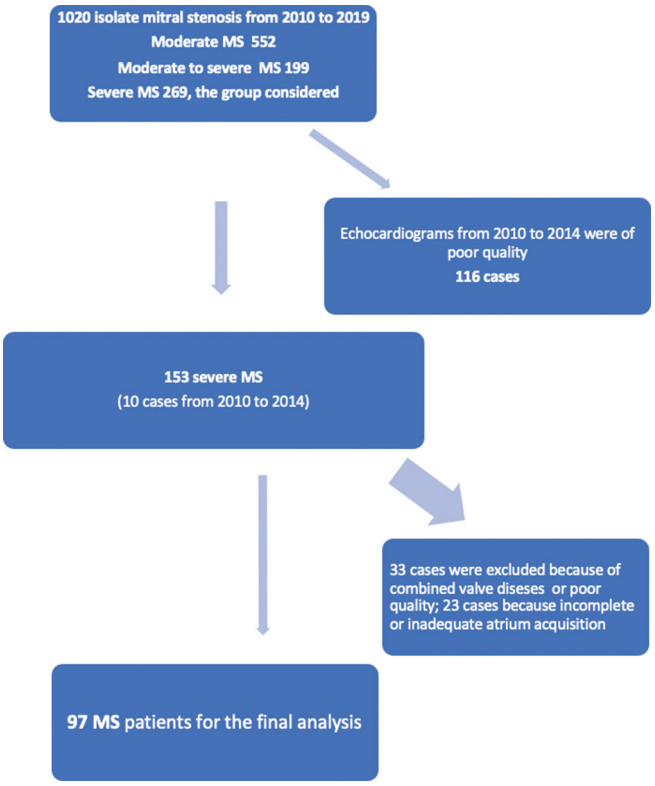


Figure 1: Flowchart describes the derivation of the study population

Right ventricular strain

RV myocardial deformation was assessed as longitudinal strain utilizing the RV-focused apical 4CH view [Figure 3b]. The ROI of the RV was defined by accurate tracing of the endocardial border, which was the inner contour of the myocardium, paying attention that the apex was included during the entire cardiac cycle, the trabeculae were excluded as was the moderator band. The free wall strain (RV-fwLS) and the RV global strain (RV-GLS) was calculated by the Tomtec software. Endocardial tracking was considered[10,12] [Figure 4].

Echocardiographic measures of right ventricular-arterial coupling

As the status of RV performance is better assessed by the RV length-force relationship, TAPSE/PASP was calculated as a representative index of RV performance.[12] RV myocardial deformation, as RV-fwLS versus PASP (RV-fwLS/PASP) was also used as a marker of RV performance status.[13]

Statistical analysis

All the analyses were performed using a commercially available package (SPSS, Rel. 11.0, 2002, SPSS Inc., Chicago, Illinois, USA). Continuous values are presented as mean ± 1 standard deviation and categorical values as proportions or percentages. The relationship between continuous variables was studied using the Pearson linear correlation coefficient, including the interrelationship between mean MV gradient and LASr versus SVi, PASP, TAPSE, right S`, RV FAC, RV free wall strain. Then subjects were divided into tertiles of

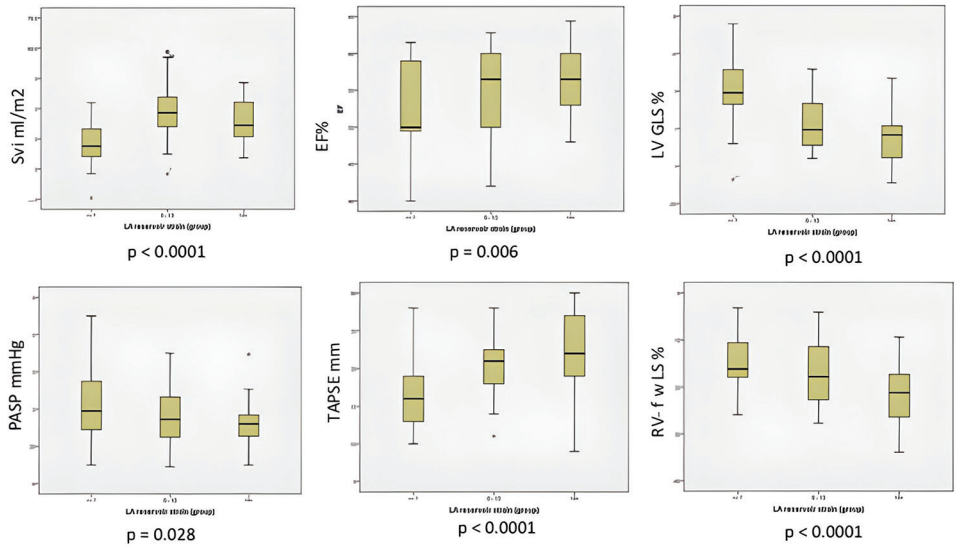


Figure 2: Box-plot of hemodynamic parameter according to LA reservoir strain tertiles. Box-plot for stroke volume index. EF: Ejection fraction, LVGLS: Global longitudinal strain of the left ventricle, PASP: Pulmonary artery systolic pressure, TAPSE: Tricuspid annular plain systolic excursion, (right ventricular free wall longitudinal strain) are represented according to tertiles of left atrial reservoir strain (Group 1:33 subjects, left atrial reservoir strain ≤7%; Group 2: 32 subjects, left atrial reservoir strain 8-13%, Group 3: 32 subjects left atrial reservoir strain ≥14%)

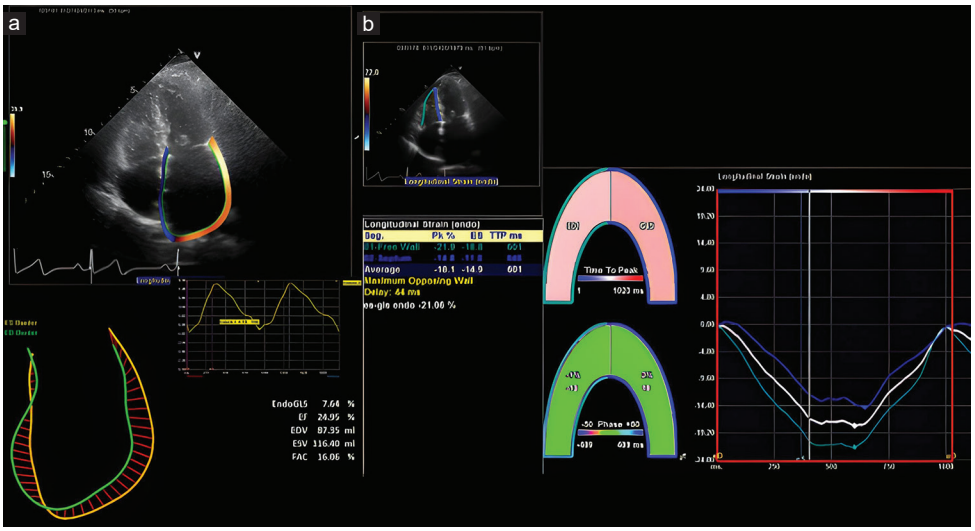
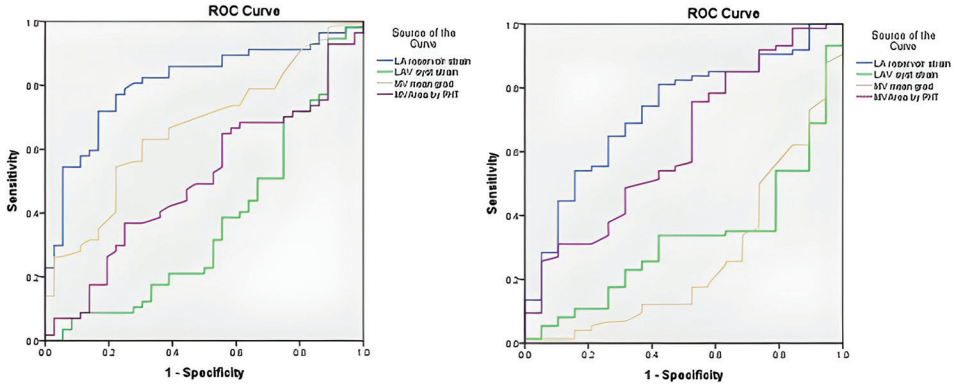


Figure 3: Strain of the left atrium and right ventricle. Tracing and strain of the left atrium, (a) and right ventricle (b) by Arena version 4.6 software



AUC for AF	Area
Test Result Variables	
LASr	0.8
LA volume	0.368
MV mean gradient	0.667
MVArea by PHT	0.503

AUC for PASP	Area
Test Result Variables	
LASr	0.726
LA volume	0.232
MV mean gradient	0.265
MVArea by PHT	0.624

Figure 4: Receiver operating characteristic for atrial fibrillation and PASP. Left atrial reservoir strain was the parameter with higher under the curve either for atrial fibrillation or PASP ≥50 mmHg (0.8 and 0.726 respectively) among the parameters tested (left atrial volume, mitral valve mean gradient, mitral valve area by pressure half time)

LASr: Group 1: LASr ≤7% (n = 33); Group 2: LASr 8%–13% (n = 32), Group 3: LASr ≥14% (n = 32). Differences between the three groups were examined using the ANOVA test for the continuous variables. Logistic multiple regression analysis was performed to test the independent relation of mean MV gradient, MV area by PHT, LAV, sex, age, and LASr with severe PASP >=50 mmHg and AFib. The area under the curve (AUC) was calculated as a representative of the relative discriminatory ability of LASr, MV mean gradient, MV area derived by PHT, and LA systolic volume as a predictors of AFib and PASP severity. The variables used were LASr, mean MV gradient, LA systolic volume, MV area calculated by PHT. A P value of 0.05 was considered statistically significant.

Missing data

Missing data was predominantly due to patients in whom echo quality was not good enough to perform offline strain analysis on. In 32 of the patients, it was not possible to read the strain of the RA. In addition, LV strain could only be measured in patients in sinus rhythm and in 10 cases, RV strain was not readable. Because of the relatively high number of cases included in this study, and the fact that this is a real-world representation of inadequacies of echo windows, we felt it was a fair representation of data in the clinical domain.

Results

Ninety-seven patients with severe isolated mitral stenosis met the inclusion criteria. Their mean age was 47.4 ± 11.9 years,

Table 1: Mean and standard deviation in all group and in tertiles of LASr

Variable	Total cohort	Group 1 (n=33) LASr ≤7%	Group 2 (n=32) LASr 8-13%	Group 3 (n=32) LASr ≥14%	P
Meeting guideline criteria for intervention based on echo data, n (%)					
Afib/SR	37/60 (38.1)	24/9 (72.7)	11/21 (34.4)	2/30 (6.2)	0.0001
PASP (mmHg) ≥50/<50	21/76 (21.6)	13/20 (39.4)	6/26 (18.7)	2/30 (6.2)	0.005
Meeting criteria for intervention No/yes	46/51 (58.7)	4/28 (87.5)	14/18 (56)	28/4 (12.5)	0.0001
Age (years)	47.4±11.9	50.4±13.6	48.4±12.3	43.7±9.1	0.07
Male/female	30/67	11/22	13/19	6/26	0.1
SBP (mmHg)	120.8±17.8	122±19.8	125±18	115±15.3	0.09
DBP (mmHg)	69.6±12.2	68±13.8	73±12.4	67±12.4	0.07
HR (bpm)	72.3±12.8	77±12	72±14	67±10	0.008
Mean MV gradient (mmHg)	8.3±5.1	8.3±5.6	8.6±5.1	7.7±4.8	0.7
MV area by PHT (cm^2)	1.35±0.3	1.35±0.38	1.34±0.36	1.35±0.33	0.9
LVMi (g/m^2)	79.2±22.2	82.6±24.8	79.6±20.5	75.1±22.1	0.4
RWT	32.7±7.3	33.1±6.2	32.9±8.2	32.2±7.7	0.8
PVR (WU)	2.08±0.8	2.5±1	2.0±0.6	1.6±0.4	0.0001
Right S` (cm/s)	10.5±2.5	8.9±1.8	11.3±2.4	11.5±2.4	0.0001
RV FAC (%)	35.6±9.1	32±9.7	38±10.6	36±5.7	0.02
RV systolic area (cm^2)	10.59±3.2	11.11±3.2	10.4±3.7	10.2±2.6	0.5
RV-fwLG/PASP (no 10 patients with severe TR)	0.63±0.4	0.48±0.4	0.62±0.5	0.78±0.4	0.05
TAPSE/PASP (no 10 patients with severe TR)	0.71±0.5	0.56±0.5	0.72±0.47	0.85±0.53	0.1
LASr (%)	11.18±6.4	4.7±1.9	10.25±2	18.8±4	0.0001
LA volume systole (ml)	128.3±48.3	146.9±54.1	133.5±43	104.7±37.4	0.001
LA volume diastole (ml)	103.9±48.4	135±51.8	106.7±37.6	70±30	0.0001
LA EF (%)	20.1±12.5	8.35±5.4	18.58±6.7	32.25±8.9	0.0001
SVR dynamic (s/cm^5)	1.77±0.69	1.97±0.66	1.65±0.8	1.69±0.45	0.1

BP: Blood pressure, SBP: Systolic BP, DBP: Diastolic BP, HR: Heart rate, MV: Mitral valve, PHT: Pressure half time, LVMi: Left ventricular mass index, RWT: Relative wall thickness, AFib: Atrial fibrillation, SR: Sinus rhythm, PASP: Pulmonary artery systolic pressure, PVR: Pulmonary vascular resistance, RV: Right ventricular, FAC: Fractional area change, RV-fwLG: Right ventricular-free wall longitudinal strain; LA: Left atrium, SVR: Systemic vascular resistance, EF: Ejection fraction, TR: Tricuspid regurgitation, TAPSE: Tricuspid annular plain systolic excursion, LASr: left atrium reservoir strain

Table 2: Simple correlation between mean mitral valve gradient, LASr and right ventricular function and stroke volume index

	Mean MV gradient		LASr	
	r	P	r	P
PASP (mmHg)	0.49	0.0001	−0.31	0.002
TAPSE (mm)	0.03	0.7	0.42	0.0001
Right S` (cm/s)	0.22	0.03	0.36	0.0001
RV FAC (%)	−0.15	0.1	0.206	0.04
RV-fwLS (%)	0.03	0.7	−0.36	0.0001
SVi (ml/m^2)	0.13	0.17	0.24	0.018

MV: Mitral valve, PASP: Pulmonary artery systolic pressure, TAPSE: Tricuspid annular plain systolic excursion, RV S`: Right ventricular longitudinal contraction by tissue Doppler imaging, RV: Right ventricular, FAC: Fractional area change, RV-fwLG: Right ventricular-free wall longitudinal strain, SVi: Stroke volume index, LASr: left atrium reservoir strain

67 (69%) being female. Their hemodynamic characteristics are summarized in Table 1. In brief, the mean gradient across the MV was 8.3 ± 5.1 mmHg and the MV area derived by PHT was 1.3 ± 0.3 cm^2. Mean LVEF was 51.79 ± 11.3%, with a corresponding SVi 34.6 ± 10.3 ml/m^2 and mean PASP was 38.1 ± 18.4 mmHg.

Twenty-one (27.6%) patients had PASP ≥50 mmHg at rest. Thirty-seven patients (38%) were in AFib at the time of the study. A LA thrombus was found incidentally in two patients: in the LA appendage in 1 patient, and in another patient was associated with intense spontaneous echo-contrast. Fifty patients had PASP >50 mmHg and/or AFib, i.e., they met guideline criteria for intervention. They were older (43.2 ± 8.8 vs. 50.6 years, P = 0.002), had larger LAV (115 ± 43 vs. 139.4 ± 50.2 ml, P = 0.015) and their LASr was significantly lower (15.19 ± 6 vs. 7.61% ± 4.4%, P < 0.0001) than those not meeting criteria for intervention. MV mean gradient, MV area derived by PHT, LVEF, SVi were similar among those needing intervention versus those not. The correlation between LASr and RV parameters was stronger than that with MV mean gradient [Table 2]. In Figure 5 are depicted the differences in hemodynamic characteristics between the various tertiles of LASr. Patients belonging to the lowest tertile of LASr had the worst LVEF, SVi, LV-GLS, TAPSE and RV adaptation, and the highest PASP.

On multivariable logistic regression analysis, LASr and mean MV gradient were the only variables that were independently associated with severity of PASP. LASr, MV mean gradient, and age were independently associated with the presence of

Table 3: Univariate and logistic multivariate backward analysis between

Univariate			Backward multivariable regression analysis				
Variable	**ß**	***P***	**Variable**	**ß**	***P***	**OR**	**CI**
Presence of AFib							
Age	0.78	0.0001		0.063	0.021	1.06	1.01-1.12
Gender	−0.2	0.6					
LA Vol	0.009	0.06					
Mean MV pressure gradient	1.29	0.13		−0.28	0.007	0.81	0.69-0.94
MVA by PHT	−0.38	0.49					
LASr	−0.228	0.0001		−0.26	0.001	0.76	0.67-0.95
Presence of PASP ≥50 mmHg							
Age	0.16	0.4					
Gender	1.15	0.027					
LA Vol	0.009	0.07					
Mean MV pressure	0.17	0.001		0.16	0.003	1.17	1.06-1.30
MVA by PHT	−1.37	0.08					
LASr	−1.56	0.005		−0.156	0.008	0.85	0.76-0.96
Presence of PASP ≥50 mmHg and/or AFib							
Age	0.08	0.6		−0.081	0.004	1.08	1.02-1.14
Gender	0.57	0.2					
LA Vol	0.01	0.02					
Mean MV pressure	0.015	0.7					
MVA by PHT	−1.01	0.08		−2.106	0.023	0.12	0.02-0.7
LASr	−0.267	0.0001		−0.272	0.0001	0.76	0.67-0.859

LA: Left atrium, MV: Mitral valve, PHT: Pressure half time, AFib: atrial fibrillation, PASP: Pulmonary artery systolic pressure, LASr: left atrium reservoir strain, MVA: mitral valve area

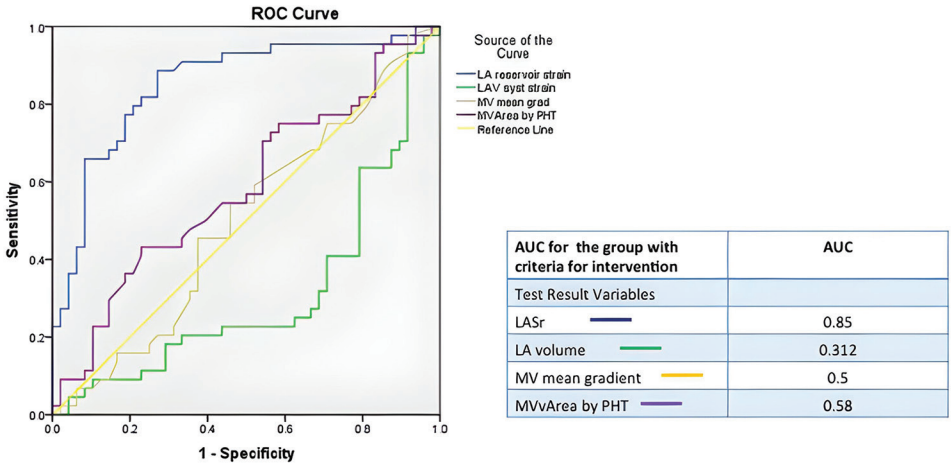


Figure 5: Receiver operating characteristic for the patients the meet the ESC 2017 criteria for mitral valve stenosis intervention left atrial reservoir strain had the higher area under the curve

AFib and LASr, MVA by PHT and age predict the group of patients that met the ESC 2017 management valvular heart disease guideline criteria for the intervention [Table 3].

Receiver operating characteristic (ROC) for LASr, MV mean gradient, MV area derived by PHT and LA systolic volume as the predictors of AFib, PASP and the group of patients that met the ESC guideline criteria for intervention are displayed in Figure 6. LASr demonstrated high sensitivity and specificity in predicting the presence of AFib (AUC 0.8), PASP (AUC 0.72), and the group with criteria for intervention (AUC 0.85, LASr of 7.7% as the best predictor point with sensitivity 0.9 and specificity 0.6) .

Discussion

In the present cross-sectional cohort study of adult patients with isolated severe rheumatic MV stenosis, we observed a strong association between LASr and PASP above 50 mm Hg, the presence of AFib and RV dysfunction. Indeed, LASr

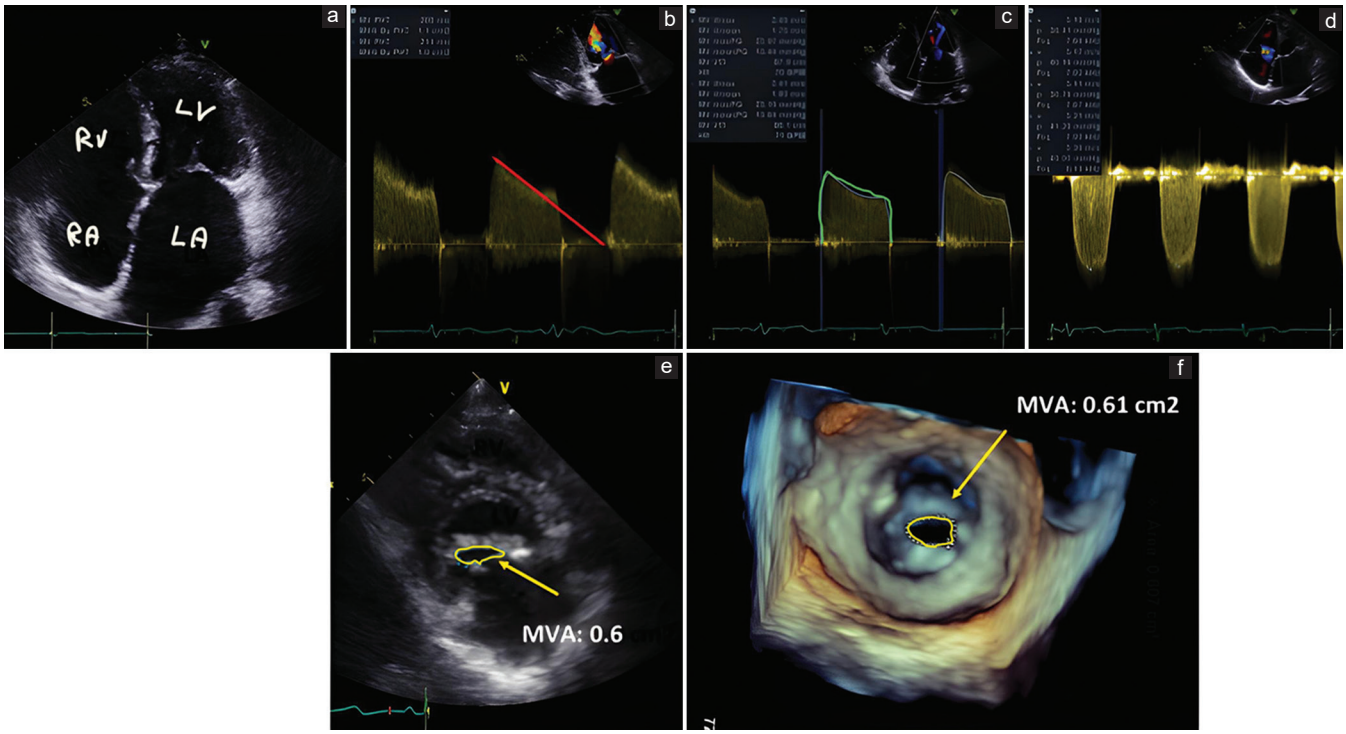


Figure 6: (a) 4 chamber view: severely dilated atria. (b) MV area was evaluated using PHT method (220/PHT) or by 2D planimetry (e) and 3D planimetry (f). (c), (d) Peak and mean mitral gradients were obtained from the apical position using CW Doppler recordings for the estimation of MV stenosis severity (peak and mean gradients)

of ≤7% also demonstrated a >80% accuracy in identifying those with PASP ≥50 mm Hg and or AFib and severe MS. These preliminary observations suggest that LASr may be a useful addendum in the surveillance of patients with isolated rheumatic MS. Future studies will need to focus on whether LASr can indeed predict future development and more specific criteria for intervention or long-term outcome.

A well-functioning LA is able to optimize the diastolic filling of the LV through its reservoir, conduit and contractile function, respectively, thereby maximizing LV SV for a given circulatory volume.[14] Pathologic processes such as rheumatic heart disease may interfere with such optimal atrial function by potentiating atrial myocytolysis, inflammation, and fibrosis,[15] as well as through the upstream hemodynamic effects of developing mitral valvular obstruction. Progressive MV stenosis produces pressure and volume load on the LA myocardium, impacting on the atrial viscoelastic state in such a way as to promote mechano-transduction that facilitates fibrosis and reduced atrial compliance with a different pathophysiology from degenerative valve involvement.[16] Kuppahally *et al*. confirmed a strong correlation between LA strain by 2D echocardiography and delayed hyperenhancement by MRI, a technique established for fibrosis identification.[17]

In the present study, we found a mean LASr values of approximately 11% in patients with severe MS, markedly reduced from the expected 45% in normal subjects,[18] and from the 20% cutoff that identifies the point where there is elevated LA pressure.[19,20] In fact, the bottom tertile of LASr exhibited atrial strain values of only 4% suggesting an immense global atrial fibrotic burden and likely significant LA hypertension.

Shenthar *et al*. examining atrial myocardial biopsy specimens from patients with severe MV stenosis undergoing MV replacement, found greater myocyte hypertrophy and glycogen deposition in those patients retaining sinus rhythm, as compared to patients in persistent AFib who had more myocytolysis.[15] The amount of fibrosis was not different between the two groups. These observations suggest that it is not only fibrosis that determines atrial function, but also the relative loss of functional myocytes that determine atrial function as assessed by global reservoir strain. This association between the MV disease, LA histopathology, and right heart decompensation has also been observed in severe mitral regurgitation.[21] Ultrastructural changes in the LA when coupled with rising LA pressure are expected to produce a relative exit block on the pulmonary circulation with consequent pulmonary hypertension which, over time may affect RV function.

In the present study, we found that 58.7% of patients with severe MV stenosis, met guideline criteria for intervention and found that the strongest associations to be MV area, age, and LASr. The ROC curve analysis showed LASr to have an excellent sensitivity and specificity profile in identifying those with PASP >50 mm Hg and the presence of AFib. We were not able to demonstrate an important association between mean MV gradient and the presence of AFib. This most likely is a consequence of the low flow state characteristic of

more advanced disease. Indeed, patients in persistent AFib were older, had lower SVi and also lower MV mean gradient. Moreover, in the group with persistent AFib and/or significant PASP ≥50, LASr was lower than those in sinus rhythm or with PASP <50 mmHg.

In the present study, adverse RV-PA coupling (RV-fwLS/PASP) was worst in the bottom tertile of LASr, declining as total pulmonary vascular afterload increased. Iacoviello *et al*. in a population with heart failure and reduced LVEF demonstrated that RV-fwLS/SPAP was independently associated with increased mortality when RV-fwLS/PASP was < 0.65.[13] Of note 2/3 of the present study population had RV-fwLS/PASP < 0.65. In addition, all parameters of RV function (TAPSE, RV S`, RV-fwLS, RV FAC) showed a close correlation with LASr.

Limitations

There are several limitations in the present study. First, it is a retrospective study, all measurements were made offline, and the echocardiograph acquisitions were not dedicated to strain assessment, i.e., we did not obtain dedicated focused views of the LA for strain measurements. It is likely therefore that the atrial were inadvertently foreshortened. Care was however taken by the investigators to avoid such confounding factors. The cohort was relatively small, and prevented broader statistical inferences. In the current iteration we did not aim to define clinical outcomes nor correlate them with the echocardiographic data. This will however be pursued with longer longitudinal follow data. The analyses of the present study focused on echocardiographic parameters and only basic clinical and demographic characteristics. This study did not include exercise stress responses, and it is likely that we did not identify all patients with abnormal pulmonary vascular physiology. We also did not use multimodality evaluation of the RV and it is likely that we did not capture all patients with RV functional impairment. Finally, we had a detailed retrospective information only for patients that were regularly followed by our institution but not for those that came from other hospitals. For this reason, AFib status was considered at the moment of transthoracic echocardiography evaluation.

Conclusions

Although rheumatic heart disease is increasingly relegated to the forgotten corridors, its impact is not small, and surgical burden is high. In severe rheumatic MV stenosis, LA mechanical function is closely associated with worse disease state and those that require intervention on the MV. Specifically, it is able to predict with great accuracy those with pulmonary hypertension, RV dysfunction, and AFib. The authors believe, the addition of LASr measurement to conventional echo assessment, and the demonstration of early decline in strain in association with severe isolated stenosis, may be able to aid decision-making with respect to surgical or transcatheter intervention, and that it is therefore a useful addendum in the ongoing surveillance of those with severe MS. Future studies are needed to identify how LASr changes longitudinally, and whether it can identify those patients with imminent decline in RV function, onset of Afib and development of RV hypertension. LASr could be also a marker for best surgical timing in terms of AFib regression and improvement in pulmonary hypertension.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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