RESEARCH

Atrial-ventricular function in rheumatic mitral regurgitation using strain imaging

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Abstract

Background: Chronic mitral regurgitation (MR) historically has been shown to primarily affect left ventricular (LV) function. The impact of increased left atrial (LA) volume in MR on morbidity and mortality has been highlighted recently, yet the LA does not feature as prominently in the current guidelines as the LV. Thus, we aimed to study LA and LV function in chronic rheumatic MR using traditional volumetric parameters and strain imaging.
Methods: Seventy-seven patients with isolated moderate or severe chronic rheumatic MR and 40 controls underwent echocardiographic examination. LV and LA function were assessed with conventional echocardiography and 2D strain imaging.
Results: LA stiffness index was greater in chronic rheumatic MR than controls (0.95 ± 1.89 vs 0.16 ± 0.13, $P = 0.009$). LA dysfunction was noted in the reservoir, conduit, and contractile phases compared with controls ($P < 0.05$). LA peak reservoir strain (ε_R), LA peak contractile strain, and LV peak systolic strain were decreased in chronic rheumatic MR compared with controls ($P < 0.05$). Eighty-six percent of patients had decreased LA ε_R and 58% had depressed LV peak systolic strain. Decreased ε_R and normal LV peak systolic strain were noted in 42%. Thirteen percent had normal ε_R and LV peak systolic strain. One patient had normal ε_R with decreased LV peak systolic strain.
Conclusions: In chronic rheumatic MR, there is LA dysfunction in the reservoir, conduit, and contractile phases. In this study, LA dysfunction with or without LV dysfunction was the predominant finding, and thus, LA dysfunction may be an earlier marker of decompensation in chronic rheumatic MR.

Key Words

- left atrium
- left ventricle
- rheumatic mitral insufficiency
- strain imaging

Introduction

Chronic mitral regurgitation (MR) results in volume overload of the left ventricle (LV) and left atrium (LA) (1). The LA compensates by increasing compliance through neurohormonal modulation and undergoing structural changes such as cellular hypertrophy and interstitial fibrosis to meet the needs of the new hemodynamic load (1, 2). The LV also undergoes similar adaptation to the increased preload (3). After a period of compensation, LA and LV dysfunction supervenes, culminating in atrial fibrillation, heart failure, and death if left untreated (4). Both the LA and LV undergo phases of compensation before reaching the lower limb of the Frank–Starling curve and irreversible remodeling (3, 5, 6, 7). In this study, we sought to simultaneously evaluate LA and

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LV function in moderate or severe chronic rheumatic mitral regurgitation (CRMR) using traditional volumetric parameters and strain imaging to answer the succeeding hypothesis. We hypothesized that the temporal sequence may differ in an individual patient – in some, the LA may transition from a phase of compensation to decompensation prior to the LV, whereas in others the reverse may occur – depending on a variable combination of preload, afterload, and intrinsic characteristics of the two chambers. Therefore, the alteration in some patients' LA functional indices may serve as an early sign heralding the onset of a decompensated state. This may occur even in the presence of normal LV functional indices and absence of symptoms (2). Further, in rheumatic heart disease, we suspect that the LA hemodynamics will differ in comparison with the LA in MR due to other etiologies, secondary to involvement of the LA as part of the rheumatic pancarditis process (8, 9, 10, 11). Additionally, the impact of preoperative dual chamber dysfunction may confer greater postoperative morbidity and mortality than isolated LV or LA dysfunction. Thus, limiting surgical indications to predominantly LV parameters may result in missing the opportunity to intervene early.

Methods

This was a prospective cross-sectional study at Chris Hani Baragwanath Academic Hospital. Patients were enrolled from January 2014 through October 2014. All study patients gave written informed consent. All patients were screened, and patients deemed to have moderate or severe CRMR were referred for possible inclusion in the study. Ninety-one patients with presumed CRMR underwent clinical evaluation, resting ECG, and detailed echocardiographic assessment according to a predetermined protocol.

Inclusion criteria were age 18 years or older and echocardiographic features of moderate or severe CRMR.

Patients were excluded if any of the following comorbidities were present: significant aortic valve disease, concurrent mitral stenosis with a valve area of <2.0 cm^2, documented ischemic heart disease, pre-existing nonvalvular cardiomyopathy, prior cardiac surgery, congenital or pericardial disease, pregnancy, severe systemic disorders such as renal failure, uncontrolled hypertension (systolic blood pressure >140 mmHg, and diastolic blood pressure >90 mmHg) on medication, or severe anemia (hemoglobin <10 g/dL).

Fourteen patients were excluded because of the following: atrial fibrillation ($n=2$), anemia ($n=2$), renal dysfunction ($n=3$), mild MR ($n=2$), MR of non-rheumatic etiology ($n=3$), and inadequate image quality ($n=2$). The final sample included 77 patients.

Forty age- and sex-matched controls were also included. Subjects were recruited from unrelated staff at Baragwanath Hospital and volunteers who presented themselves to the echocardiography laboratory following an advertisement about this study. The inclusion criteria were absence of symptoms, normal blood pressure (≤140/90 mmHg), absence of diabetes and cardiovascular disease, absence of chronic medication, and presence of sinus rhythm (heart rate between 50–85 beats/min). The exclusion criteria were abnormal 12-lead ECGs, abnormal screening echocardiograms, and suboptimal image quality.

The study was approved by the University of the Witwatersrand Ethics Committee (M140114) and complies with the Declaration of Helsinki.

Transthoracic echocardiography was performed on all patients in the left lateral position by experienced sonographers using an S5-1 transducer on a Philips iE33 system. Images were obtained according to a standardized protocol (12). Data were transferred and analyzed offline using the Xcelera workstation (Philips).

All linear chamber measurements were performed according to the American Society of Echocardiography (ASE) chamber quantification guidelines (13). Maximum LA volume (LA_{max}) was obtained at LV end-systole from the 2D frame, just before the opening of the mitral valve (MV) (14, 15). Pre-atrial volume ($V_{pre\text{-}A}$) was obtained from the diastolic frame, just before the MV reopened as the result of atrial contraction (15). LA minimum volume (LA_{min}) was assessed at LV end-diastole, utilizing the smallest volume seen after LA contraction (14, 15).

LA phasic function assessment was done by using the following formulas:

1) *Reservoir function:* LA emptying fraction (LAEF) total = $(LA_{max} - LA_{min}/LA_{max}) \times 100\%$; expansion index = $(LA_{max} - LA_{min}/LA_{min}) \times 100\%$
2) *Conduit function:* passive emptying volume (PEV) = $(LA_{max} - V_{pre\text{-}A})$; passive LA emptying fraction (LAPEF) = $LA_{max} - V_{pre\text{-}A}/LA_{max} \times 100\%$; and conduit volume = LV stroke volume – $(LA_{max} - LA_{min})$
3) *Booster pump function:* LA active emptying fraction (LAAEF) = $(LA_{pre\text{-}A} - LA_{min})/LA_{pre\text{-}A}) \times 100\%$; LA active emptying volume (LA active EV) = $(V_{pre\text{-}A} - LA_{min})$ (14, 15)

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All LA volumetric parameters were indexed to body surface area (BSA) (15).

LV end-diastolic volume, end-systolic volume (ESV), and ejection fraction (EF) were assessed using the Simpson's method and indexed to BSA (13). Measurements relating to LV diastolic function were performed in accordance with the ASE guidelines on diastolic function and included pulsed-wave Doppler at the mitral tips and tissue Doppler of both the medial and lateral mitral annuli (16). Measurements relating to the right ventricle (RV) were based on the ASE guidelines on the RV (17).

MR was considered rheumatic in etiology when the morphology of the valve satisfied the World Heart Federation criteria for the diagnosis of chronic rheumatic heart disease (18). MR severity was assessed using qualitative, semi-quantitative, and quantitative methods as per the ASE and European Society of Cardiology valvular regurgitation guidelines (19, 20). In equivocal cases, echocardiographic data were integrated with the clinical evaluation by an experienced cardiologist to distinguish moderate from severe MR.

Apical four- and two-chamber views were obtained using 2D greyscale echocardiography for speckle-tracking analysis (15, 21). This was performed during end-expiratory breath-hold and stable ECG recording (14, 15, 21). An adequate greyscale image that allowed separation of myocardial tissue and surrounding structures was obtained. Three consecutive cardiac cycles were recorded and averaged. The frame rate was set between 60 and 80 frames per second. Philips QLAB version 9.0 software allowed offline semi-automated analysis of speckle-based strain. The endocardial surface of the LA was traced manually in both the four- and two-chamber views by a three-point-and-click approach. The system then automatically generated an epicardial surface tracing (15). The region of interest (ROI) was thus created and manually adjusted as needed to allow for adequate speckle tracking.

The QLAB 9 speckle-tracking software divides the ROI into seven segments in the two- and four-chamber views. It then generates the ε curves for each myocardial segment and subsequently an average curve of all segments (15). From these strain curves, the peak LA ε_R and contractile phase (ε_{CT}) were calculated. The peak reservoir strain of the LA was measured at LV end-systole, and the peak LA contractile strain was measured at the onset of atrial contraction (Fig. 1).

Two-dimensional echocardiographic images were obtained at end-expiration from LV apical long-axis four-, three-, and two-chamber views with frame rates between 60 and 80 frames per second (22). Three consecutive cardiac cycles were recorded and averaged (23). Peak LV longitudinal systolic strain (LVPSS) was calculated for apical long-axis views, and global LV systolic strain was calculated by averaging the three apical views as previously described (22, 24).

Four categories were created to make an assessment of simultaneous LA and LV function using peak global LA strain (LA ε_R) and peak global LV strain (LVPSS). These categories comprised patients with normal LA ε_R and LVPSS (category 1), normal LA ε_R with decreased

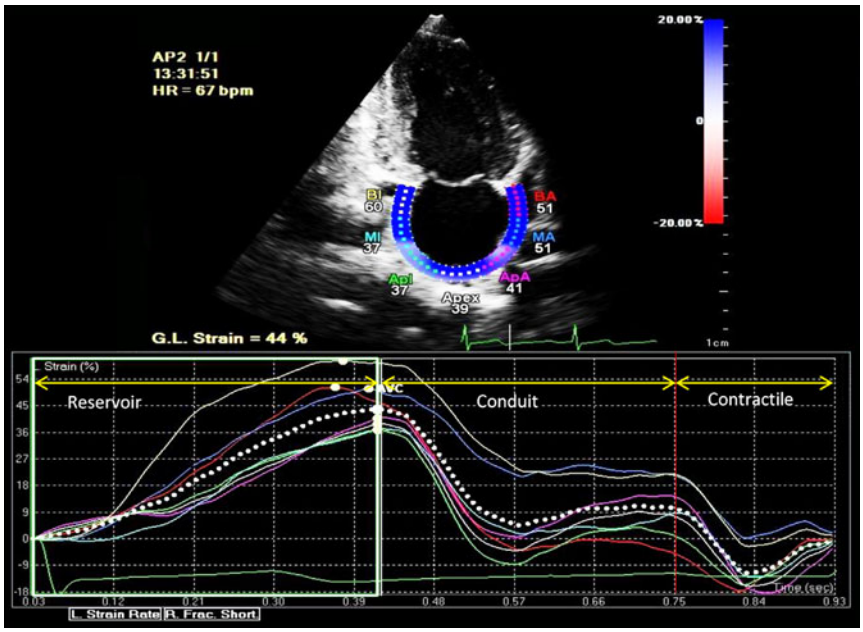

Figure 1
Apical two-chamber view of the left atrium depicting reservoir, conduit, and contractile phases.

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LVPSS (category 2), decreased LA ε_R and LVPSS (category 3), and decreased LA ε_R and normal LVPSS (category 4).

The LA stiffness index was calculated noninvasively as the ratio of E/E′ lateral and LA ε_R (25, 26).

Statistical analysis was performed with Statistica, version 12.5, series 0414 for Windows. Continuous variables are expressed as mean±s.d. or median (interquartile range). Student's *t*-test or Mann–Whitney *U* test were used to compare continuous variables. Categorical variables were evaluated by chi-square and Fisher's exact test when necessary.

Intraobserver and interobserver variability were assessed for peak positive LA ε_R, peak negative LA ε_{CT}, and LVPSS. Measurements were taken in 20 randomly selected subjects from the control group. To assess interobserver variability, two independent observers measured the LA volumetric and strain parameters (LA and LV), and intraobserver variability was calculated from the analysis of the same observer after 1 month of the first measurement. Interobserver and intraobserver reproducibility were assessed by calculating coefficients of variation, which were calculated as the s.d. of the differences divided by the mean. A paired *t*-test was used to compare the mean and s.d. of the values derived for strain within the control group and for LA volumes in the control group and to calculate the significance value. A P value of <0.05 was considered statistically significant.

Results

Clinical and echocardiographic characteristics of the study and control populations are shown in Table 1. The control arm and MR patients showed no significant difference with regard to age, sex, BMI, blood pressure, and heart rate. Moderate MR was present in 51 patients (66%) and severe MR was present in 26 (34%). LA and LV diameters and volumes were increased in the study patients compared with controls ($P<0.05$). Surrogates of LV systolic function were worse in CRMR than in controls (S′ medial: 6.3±1.3 cm/s vs 7.1±1.6 cm/s, $P=0.004$; ESV indexed: 40.0±22.2 mL/m² vs 17.8±6.4 mL/m², $P<0.0001$). Patients with CRMR had a higher E/E′ ratio than the controls (E/E′ medial ratio: 20.1±10.7 vs 9.4±3.0, $P<0.0001$) as a result of higher E wave velocity (133.8±48.1 vs 77.0±17.6, $P<0.0001$). However, there was no difference in the EF between the group with MR and controls ($P=0.07$).

LA phasic volumes and functional analysis are summarized in Table 2. LA_{max}, LA_{min}, and $V_{pre\text{-}a}$ were higher in the study patients than controls ($P<0.0001$). However, the indices of reservoir, conduit, and contractile function were all depressed in the study patients compared with the controls ($P<0.001$). LA stiffness index was greater in the MR patients than the controls (0.95±1.89 vs 0.16±0.13, $P=0.009$).

LA and LV strain parameters are indicated in Fig. 2 and Table 2. LA ε_R, LA ε_{CT}, and LVPSS were decreased in the MR group compared with the controls ($P=0.04$) (Table 2). Eighty-six percent of MR patients had decreased LA ε_R (Fig. 2). Fifty-eight percent had depressed LVPSS. Thirteen percent had normal LA ε_R and LVPSS (category 1). One patient had normal LA ε_R with decreased LVPSS (category 2). Decreased LA ε_R and LVPSS were present in 44% of patients (category 3). Decreased LA ε_R and normal LVPSS were noted in 42% of patients (category 4). The aforementioned categories are depicted in Fig. 3. In patients with mitral regurgitation, there was an overall positive correlation between LA and LV peak systolic strain ($r=0.47$, $P<0.001$).

The intraobserver coefficient of variation for LA ε_R was 4.8% with a mean difference of 3.2±0.67 ($P=0.3$) and for LA ε_{CT} was 4.6% with a mean difference of 1.43±0.31 ($P=0.3$). The interobserver variability coefficient was 9% for both LA ε_R ($P=0.6$) and ε_{CT} ($P=0.6$) with mean differences of 3.2±0.35 and 1.2±0.13, respectively.

The intraobserver coefficient of variation for LVPSS was 2.4% with a mean difference of 1.1±2.7 ($P=0.09$). The interobserver variability coefficient for LVPSS was 9.8% with a mean difference of 0.25±2.4 ($P=0.6$).

Discussion

The main findings of this study are:

1) Absolute volumes of the LA increase compared with normal controls during the three phases, whereas the relative percentage change in volume is diminished in all phases.
2) Both LA ε_R and ε_{CT} were decreased in the study group compared with normal individuals.
3) LA ε_R was abnormal in the majority of patients (86%); of these, almost half (44%) had concomitant diminished LVPSS.

The LA has three main functions, namely the reservoir, conduit, and contractile functions (27). In the reservoir phase, the LA receives blood from the pulmonary veins during LV systole; in the conduit phase, there is passive emptying of blood into the LV during early diastole; and in the contractile phase, the LA actively ejects blood

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Table 1 Clinical and echocardiographic characteristics of study patients.

Variable	Study patients (n = 77)	Controls (n = 40)	*P* value
Clinical			
Age (years)	44 ± 13.6	42 ± 13.4	0.4
Sex (male:female)	13:64	8:32	0.6
BSA (m^2)	1.7 ± 0.2	1.8 ± 0.2	0.01
BMI (kg/m^2)	27.1 ± 5.9	28.4 ± 6.2	0.3
SBP (mmHg)	124.2 ± 11.4	124 ± 12.5	0.93
DBP (mmHg)	77 ± 9.1	75.7 ± 12.6	0.52
Heart rate (beats/min)	77.1 ± 12.6	76.3 ± 14.1	0.75
NYHA (I/II/III) (%)	42/49/9	-	
Hypertension (%)	40	-	
HIV (%)	13	-	
Hypertension and HIV (%)	15	-	
Echocardiographic			
LVEDD (mm)	54.8 ± 9.4	42.5 ± 4.8	<0.0001
LVESD (mm)	41.4 ± 9.4	27.1 ± 4.2	<0.0001
IVSD (mm)	8.6 ± 2.1	9.5 ± 1.9	0.02
LVPWD (mm)	8.5 ± 1.5	9.2 ± 1.9	0.03
EDVi (mL/m^2)[a]	93.2 ± 30.1	47.9 ± 13.5	<0.0001
ESVi (mL/m^2)[a]	40.0 ± 22.2	17.8 ± 6.4	<0.0001
LAVi (mL/m^2)[a]	64.1 ± 39.9	21.9 ± 4.9	<0.0001
LVEF (%)	58.5 ± 12.9	62.8 ± 11.2	0.07
LVMi (kg/m^2)[a]	102.7 ± 36.3	65.6 ± 20.3	<0.0001
E wave (cm/s)	133.8 ± 48.1	77.0 ± 17.6	<0.0001
A wave (cm/s)	98.4 ± 33.5	59.6 ± 13.0	<0.0001
Deceleration time (ms)	214.5 ± 62.2	135.4 ± 42.3	<0.0001
E/A ratio	1.5 ± 0.6	1.3 ± 0.4	0.06
E′ medial (cm/s)	7.3 ± 2.3	8.8 ± 2.8	0.002
E′ lateral (cm/s)	10.1 ± 4.0	13.4 ± 3.6	<0.0001
E/E′ medial (cm/s)	20.1 ± 10.7	9.4 ± 3.0	<0.0001
E/E′ lateral (cm/s)	15.4 ± 8.8	5.9 ± 1.6	<0.0001
S′ medial (cm/s)	6.3 ± 1.3	7.1 ± 1.6	0.004
S′ lateral (cm/s)	7.3 ± 2.5	8.2 ± 2.6	0.07
PASP (mmHg)	35.1 ± 16.9	21.5 ± 6.4	<0.0001

Data presented as mean ± S.D. or %.

[a]Values are indexed to BSA.

BSA, body surface area; DBP, diastolic blood pressure; EDVi, end-diastolic volume indexed; ESVi, end-systolic volume indexed; HIV, human immunodeficiency virus; IVSD, interventricular septal diameter; LAVi, left atrial volume indexed; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVMi, left ventricular mass indexed; LVPWD, left ventricular posterior wall diameter; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; SBP, systolic blood pressure.

into the LV in late diastole (27). MR is characterized by systolic volume overload of the LA (4, 28). In this study, volumetric measures of global LA function were increased, namely LA_{max}, LA_{min}, and $V_{pre\text{-}a}$. The increased LA_{max} would be expected secondary to systolic volume overload of the LA as a result of MR that occurs in addition to the normal venous return from the pulmonary veins. An increased $V_{pre\text{-}A}$ and LA_{min} similar to that found in prior studies was noted in the present study (1, 4, 28, 29). However, there appear to be discrepancies in the literature with regard to whether the three phasic LA volumes are increased (1, 4, 28, 29). Borg *et al.*, Yurdakul *et al.*, and Ren *et al.* found an increment in the percentage change of reservoir LA volumes with preserved booster function based on volumetric indices (4, 29, 30). In contrast, both in our study and in those of Aksakal *et al.* and Moustafa *et al.*, a relative decrement in reservoir and booster function was observed (1, 28). Of the three phases, the conduit function was preserved or increased in all the studies (1, 4, 28, 29, 30). It is possible that the similarities and differences in the phasic LA functional parameters in these studies may be attributed to a variable combination of duration and severity of MR, LV compliance, LA compliance, and the intrinsic characteristics of the LA and the LV (1, 4, 28, 29, 30, 31, 32).

It is likely that findings from the present study may relate to altered LA and LV pathophysiology in MR. In the patient exhibiting compensation with significant MR, LV diastolic function would be expected to be normal or increased to accommodate the increased blood volume

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Table 2 Left atrial and ventricular peak systolic strain and left atrial volumetric and phasic functional parameters in chronic rheumatic mitral regurgitation.

Variable	CRMR (n = 77)	Control (n = 40)	P value
Volumes			
Maximum LAVi (mL/m²)[a]	64.1 ± 39.9	21.9 ± 4.9	<0.0001
Minimum LAVi (mL/m²)[a]	39.6 ± 35.5	8.1 ± 3.1	<0.0001
Pre-A LAVi (mL/m²)[a]	49.4 ± 39.0	13.6 ± 4.6	<0.0001
Reservoir function			
LA total emptying volume indexed (mL/m²)[a]	24.6 ± 13.7	15.6 ± 12	<0.001
LAEF total (%)	45.4 ± 16.5	61.2 ± 12.0	<0.0001
LA exp index (%)	98.6 ± 62.6	194.4 ± 131.8	<0.0001
Conduit function			
LAPEVi (mL/m²)[a]	14.9 ± 13.4	8.2 ± 4.4	0.003
LAPEF (%)	26.7 ± 19.4	38.3 ± 14.9	0.001
Conduit volume (mL/m²)[a]	28.8 ± 21.6	16.7 ± 9.8	<0.001
Booster function			
LA AEF (%)	24.1 ± 13.1	38.6 ± 13.4	<0.0001
LA AEVi (mL/m²)[a]	9.7 ± 6.3	4.9 ± 2.8	<0.0001
Strain parameters			
ε_R (%)	20.7 ± 10.0	39.0 ± 7.3	<0.0001
ε_{CT} (%)	−0.5 ± 1.6	−2.28 ± 2.05	<0.0001
LV global peak systolic strain (%)	−16.1 ± 5.3	−17.9 ± 2.1	0.04
Left atrial stiffness index	0.95 ± 1.89	0.16 ± 0.13	0.009

Data presented as mean ± S.D.

[a]Values are indexed to body surface area.

CRMR, chronic rheumatic mitral regurgitation; ε_{CT}, peak left atrial strain in the contractile phase; ε_R, peak left atrial strain in the reservoir phase; LA, left atrial; LA AEF, LA active emptying fraction; LA AEVi, left atrial active emptying volume index; LA exp index, left atrial expansion index; LAEF, left atrial emptying fraction; LAPEF, left atrial passive emptying fraction; LAPEVi, left atrial passive emptying volume index; LAVi, left atrial volume index; Pre-A LAVi, pre-atrial contraction left atrial volume index.

that is required to enter the LV. This ultimately causes an increase in LV end-diastolic volume, the essential step in the path to LV diastolic overload. Thus, atrial volumetric markers of conduit and booster function would be normal or even potentially relatively increased. Conversely, in the decompensated state, impaired LV systolic function will result in significant diastolic dysfunction and a high LV end-diastolic pressure that would then impair LV diastolic filling and result in higher LA volumes during these phases. The increased LA $V_{pre\text{-}a}$ and LA_{min} observed in this study imply that atrial filling of the LV during diastole is impaired. This implies that pan-diastolic LV diastolic dysfunction can occur in patients with normal LVEF and in the absence of overt clinical LV failure. Thus, the atrial volumetric markers in diastole may serve as surrogates for impaired LV diastolic dysfunction in compensated MR patients. Prior studies and the recent ASE guidelines on LV diastolic dysfunction accentuate the difficulties of utilizing conventional mitral inflow Doppler and annular tissue Doppler parameters in MR (33). Identifying this pathophysiological phase may be important because it implies that the diastolic compliance of the LV may become affected, resulting in suboptimal early filling as reflected by impairment during the conduit phase. However, with an impairment in LV diastolic early relaxation, atrial booster function would be expected to increase, resulting in a greater proportion of filling in late diastole, as is observed in patients with LV grade 1 diastolic dysfunction as a result of other causes, for example, hypertension. This expected increment in booster function does not occur, and this must imply either severe LV diastolic dysfunction with abbreviated late diastolic filling of the LV due to high LV late diastolic pressure or the coexistence of intrinsic LA contractile dysfunction. The former postulate is supported by the high E/E′ noted in patients with MR in this study. The latter postulate may be the result of fibrosis of the LA, which contributes to LA dysfunction and may be attributed to three potential factors: aging, chronic volume overload, and the rheumatic pancarditis process itself (1, 8, 9, 10, 11, 28, 31, 32, 34, 35).

We noted a decrease in LA ε_R and ε_{CT} in the majority of the patients. Similarly, some studies report that strain during the reservoir phase increases with preserved booster strain in MR compared with a normal heart (4). These differences relate to all the reasons proposed for our volumetric findings. In this study, the decrease in ε_R can be explained as follows: (1) an increase in initial length may be expected in this cohort due to increased LA minimum

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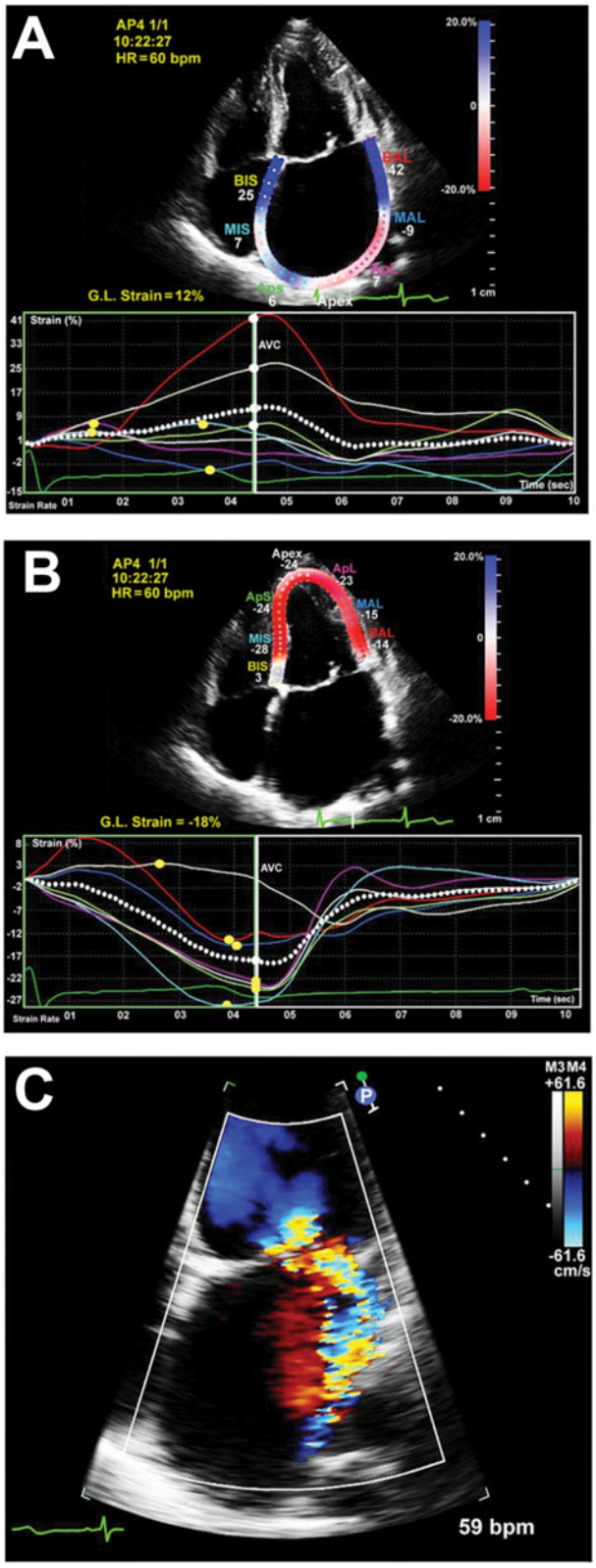

Figure 2
Decreased left atrial peak systolic strain (A) and preserved LV peak systolic strain (B) in a patient with severe rheumatic mitral regurgitation (C).

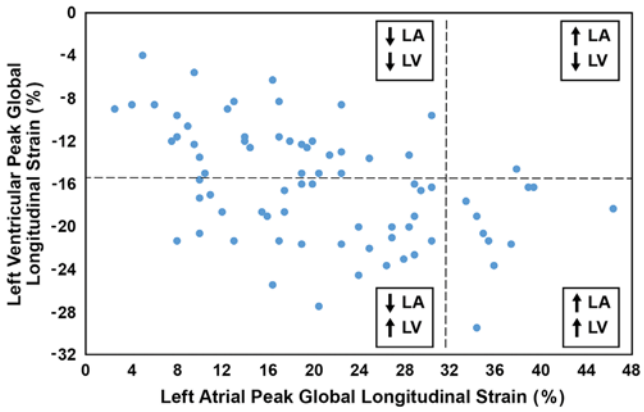

Figure 3
Four categories of left atrial (LA) and left ventricular (LV) strain were identified in patients with chronic rheumatic mitral regurgitation. Thirteen percent had normal LA ε_R and peak LV longitudinal systolic strain (LVPSS) (category 1). One patient had normal LA ε_R with decreased LVPSS (category 2). Decreased LA ε_R and LVPSS were present in 44% of patients (category 3). Decreased LA ε_R and normal LVPSS were noted in 42% of patients (category 4).

volume and (2) a decrease in the final length may be due to the decrease in mitral annular systolic descent that we observed. The latter may reflect LV longitudinal systolic impairment in MR (36, 37, 38, 39).

A second hypothesis is that intrinsic LA compliance is impaired, as evidenced by the increased LA stiffness index. Therefore, despite an increase in LA_{max} and LA_{min}, and thus the reservoir volume, the peak ε_R does not increase as expected owing to a limitation in the ability of the atrial wall to stretch in response to volume overload, as in the studies by Borg *et al.* and Yurdakul *et al.* (30). This, as supported by histopathology and MRI studies (31, 32), implies that the same pathophysiological process impairing relaxation of the atria (for example fibrosis) may be responsible for intrinsic abnormal atrial contractile function.

In chronic moderate or severe MR, the two main patterns noted were depressed LA reservoir strain with either normal or depressed LVPSS. This implies that LA function may decline in some patients before a decrement in LV longitudinal function occurs. This must relate to different clinical profiles among patients for the same degree of MR, for example, age-related or intrinsic abnormality of the LA compared with the LV, variable degrees of atrial fibrosis and energetics, and possible variation in neurohumoral factors. A further observation noted by Dardas *et al.* suggests that a state of decreased atrial contraction exists prior to surgery and that LA contractile performance improves after surgery even in patients with normal LVEF (40).

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Thus, these four categories may serve as a guide to help in risk stratification of patients with MR according to LA and LV function prior to surgical intervention.

Our study had the following limitations: Diagnostic coronary angiogram and right and left heart catheterization were performed only on patients with an indication for surgery, MR severity was not confirmed by another modality such as cardiac MRI or 3D echocardiography, and concurrent LA and LV invasive pressures were not obtained. Finally, detailed echocardiographic assessment of LV diastolic function was not performed.

Conclusion

In CRMR, analysis of volumetric indices and strain of the LA and LV indicate that there are variable combinations of LA and LV dysfunction. The decline in LA function was related to dysfunction of the reservoir, conduit, and contractile phases and represents probable LV diastolic impairment initially. A decline in LA strain can precede a decline in LV strain and thus may suggest that LA dysfunction precedes LV systolic impairment in CRMR.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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