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Assessment of the left atrial longitudinal myocardial function by the strain and strain rate echocardiography in patients with rheumatic mitral stenosis*

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Aim: To evaluate the regional left atrial (LA) myocardial functions and time to peak deformations by the longitudinal strain (S) and strain rate (Sr) echocardiography in isolated mitral stenosis (MS) patients for 3 LA periods (contractile, reservoir, and conduit periods).

Materials and methods: Included in the study were 30 MS patients and 30 healthy controls. Longitudinal peak S and Sr indices, time to peak S and time to peak Sr, and systolic and diastolic velocities were measured from the color Doppler myocardial imaging data, for each LA period.

Results: For all 3 periods, all of the segment S values and most of the segment Sr values were significantly lower in the patients than in the controls ($P < 0.0001$ and $P < 0.05$, respectively). There were no significant differences between the groups in terms of velocities. Time to peak S in the contractile and conduit periods was significantly higher in the patients than in the controls, in most of the segments ($P < 0.05$). Time to peak Sr was significantly higher in the patients than in the controls, in all of the periods in all of the segments ($P < 0.05$) except for mid-septal segments.

Conclusion: This study demonstrated that LA longitudinal myocardial functions were impaired in MS patients with S/Sr echocardiography. Our study is the first to demonstrate prolonged time to peak S/Sr of the LA in rheumatic MS. This condition might be an additional factor in the deterioration of regional LA myocardial function in MS patients.

Key words: Mitral stenosis, echocardiography, left atrial functions, longitudinal strain, strain rate

Romatizmal mitral darlıklı hastalarda strain ve strain rate ekokardiyografi ile sol atriyal longitudinal miyokardiyal fonksiyonların değerlendirilmesi

Amaç: Saf mitral darlıklı (MD) hastalarda her üç sol atriyal (SA) dönem (kontraktil, rezervuar ve konduit) için strain (S) ve strain rate (Sr) ekokardiyografi ile bölgesel SA miyokardiyal fonksiyonların ve zirve deformasyon sürelerinin değerlendirilmesidir.

Yöntem ve gereç: Çalışmaya 30 MD'li hasta ve 30 sağlıklı kontrol alındı. Her bir dönem için longitudinal zirve S ve Sr değerleri, zirve S ve Sr süreleri ile sistolik ve diyastolik velositeler renkli Doppler miyokardiyal görüntüleme verilerinden ölçüldü.

Bulgular: Her üç dönem için tüm segmentlerde S değerleri ve segmentlerin çoğunda Sr değerleri hastalarda kontrollere göre daha düşüktü (sırası ile $P < 0,0001$ ve $P < 0,05$). Velositeler açısından gruplar arasında fark yoktu. Zirve S süresi segmentlerin çoğunda kontraktil ve koduit dönemlerde hastalarda kontrole göre daha yüksekti ($P < 0,05$). Zirve Sr süresi

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orta-septal segmentler dışındaki tüm segmentlerde bütün dönemler için hastalarda kontrollere göre daha yüksekti (P < 0,05).

Sonuç: Bu çalışmada MD'li hastalarda SA logitudinal miyokardiyal fonksiyonların bozulduğu S/Sr ekokardiyografi ile gösterilmiştir. Bizim çalışmamız romatizmal MD'de SA zirve S/Sr sürelerinin uzadığını gösteren ilk çalışmadır. Bu durum MD'li hastalarda bölgesel SA miyokardiyal fonksiyonların bozulmasında ek bir faktör olabilir.

Anahtar sözcükler: Mitral darlık, ekokardiyografi, sol atriyum fonksiyonları, longitudinal strain, strain rate

Introduction

The predominant cause of mitral stenosis (MS) is rheumatic fever. The combination of mitral valve disease and atrial inflammation, secondary to rheumatic carditis, causes left atrial (LA) dilation, fibrosis of the atrial wall, and disorganization of the atrial muscle bundles (1). These changes significantly affect the LA functions. LA functions are important for the clinical course and prognosis of patients with MS. The LA myocardial mechanical cycle is composed of contractile (CP), reservoir (RP), and conduit (COP) periods. CP was defined as the A-wave duration on the pulse wave Doppler trace; RP, as the interval between the mitral valve closure and the mitral valve opening; and COP, as the interval between the mitral valve opening and the onset of the A-wave (2). Through these sequential and synchronized functions, LA contributes to left ventricular (LV) filling. LV systole occurs during RP. COP corresponds to LV early filling, to diastasis, and to LA electromechanical coupling (2).

Noninvasive assessment of LA functions has been performed by conventional echocardiography (CE), tissue Doppler imaging (TDI) technique, cardiac magnetic resonance imaging, radionuclide methods, computed tomography, and invasive angiography (3-6). However, there is no widely accepted gold standard set of parameters for LA functions. Both differentiation and quantification of regional LA myocardial functions in the 3 LA periods, one by one, are not possible by the CE.

Strain (S) and strain rate (Sr) echocardiography, which are novel quantitative techniques, used for the assessment of heart functions, originated from the tissue Doppler imaging (TDI) technique. Moreover, S/Sr imaging may overcome the major limitations of the TDI technique (tethering, neighboring tissue effects, and the rotation motion of the heart). Strain defines the myocardial deformations, and Sr defines the rate of deformation (7). The time to peak deformation (S/Sr) is important for atrial and ventricular functions; however, to date, there are no data about these indices for LA in MS patients. Recently, atrial S/Sr obtained from the TDI has been applied to regional LA function assessment (2,8-10). So far, there are no studies on S/Sr indices and time to peak S/Sr to assess LA functions in MS patients for the 3 LA periods to be evaluated, one by one. Therefore, the aim of the present study was the assessment of the regional LA longitudinal myocardial functions and time to peak deformation by S/Sr echocardiography in patients with isolated rheumatic MS for the 3 periods, one by one.

Materials and methods

The study subjects were 30 isolated rheumatic MS patients (mean age 41 ± 7.9 years; 19 women) who had normal LV functions and 30 healthy control subjects (mean age 42 ± 6.4 years; 20 women). All of the participants were in sinus rhythm, and the New York Heart Association functional class I or II. Exclusion criteria included a moderate to severe mitral regurgitation, significant disease of other heart valves, diabetes mellitus, hypertension, ischemic heart disease, heart failure, LV ejection fraction (LVEF) <50%, bundle branch block or atrial fibrillation, use of cardiac medications (diuretics, beta blockers, and vasodilators), New York Heart Association functional class III or IV, and inadequate echogenity. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local ethics committee. All of the patients and the controls were informed about the study and their written consent was obtained.

Echocardiographic examination

Conventional and color Doppler myocardial imaging (CDMI) echocardiography was performed using the Vivid 7 ultrasound system (General Electric, Horten, Norway) with a 2.5 MHz transducer. Standard 2-dimensional and M-mode echocardiographic studies were performed according to the recommendations of the American Society of Echocardiography using conventional views and measurements (11). Echocardiographic recordings involving 3 consecutive cycles were obtained from standard parasternal long-axis and apical 4- and 2-chamber views at a left lateral decubitus position. All of the recordings were stored on digital media for later measurements (Echopac PC workstation, GE). The arithmetic mean of 3 measurements was taken into consideration. LVEF was calculated using a modified Simpson's rule and Teichholz method. LA dimensions were measured from the anteroposterior in the parasternal long-axis view and the superior-inferior and mediolateral planes were measured from the apical 4-chamber view at the end systole, as previously described (12). The LA volumes were calculated according to the biplane method of discs, from the apical 4- and 2-chamber views at the onset of the P wave on the electrocardiography (pre-atrial contraction volume, Vp), just before the mitral valve opening (maximal volume, Vmax), and at the mitral valve closure (minimal volume, Vmin) (2,4). These values were corrected by body surface area. For the assessment of LA functions, the indices calculated from the volumes were used: LA stroke volume (Vs) = Vmax – Vmin, LA ejection fraction (LAEF) = (Vs/Vmax) × 100, LA expansion index (LAEI) = (Vmax – Vmin)/Vmin × 100, LA active emptying fraction (LAAEF) = (Vp – Vmin)/Vp × 100, LA passive emptying fraction (LAPEF) = (Vmax – Vp)/Vmax × 100 (2,4,8,13). The mitral valve area was calculated by the pressure halftime method and planimetry, and the mean value of these 2 measurements was determined as the mitral valve area. The velocity time integral of the A-wave was measured from the TDI recording at the lateral (AVTIL) and septal (AVTIS) mitral annular region.

Strain and strain rate echocardiography

For the measurement of deformation indices, the CDMI of the LA walls was acquired at the apical 4- and 2-chamber views, with a frame rate of 160-200 s^{-1} (14). The CDMI range setting was adapted in order to avoid aliasing within the image. Because of the thin atrial walls, a narrow (10 × 2 mm) sample volume was selected. During this procedure, the narrowest image sector angle (30°) possible was used to acquire the maximum frame rate. The evaluated wall was positioned in the center of the window to minimize artifactual data and realigned so that the direction of motion interrogated was parallel to the direction of the insonating beam. Saved in digital format were 3 consecutive cardiac cycles. S/Sr and velocity profiles were extracted and analyzed offline using commercial software (Echopac PC workstation, GE), as described previously (2,8-10). Longitudinal peak S, Sr, systolic velocity, and early and late diastolic velocity indices were measured from the mid and superior (roof) levels of the lateral, the inter-atrial septal, and the anterior and inferior walls of the LA, for each period (10). Additionally, time to peak S and time to peak Sr were measured from these data for contractile (T-CP); reservoir (T-RP); early (E) reservoir, late (L) reservoir, for time to peak Sr; and conduit (T-COP) periods, one by one (2). The mean value of 3 cardiac cycles was taken for all measurements.

Reproducibility of measurements

To assess intraobserver and interobserver variability, variability in the measurements of longitudinal peak systolic S, peak Sr, systolic V, early diastolic V, late diastolic V, and time to peak S/Sr were evaluated in 10 studies selected randomly. For the intraobserver variability, selected images were analyzed at a different time by an observer blinded to the results of the previous measurements. For the interobserver variability assessment, 2 independent observers performed the analyses.

Statistical analysis

The power of the study is 0.80. Continuous variables expressed as means ± standard deviation were compared using Student's t-test for independent groups. When the assumptions to use the Student's t-test were not satisfied, comparison between groups was performed using the Mann-Whitney U-test. For assessment of intra- and interobserver variability, the Bland-Altman method was used. All data analysis was performed using a commercially available statistical analysis software package (SPSS 12.0, Statistical Package for the Social Sciences, Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

The demographic and CE characteristics of the MS patients and healthy control subjects are shown in Table 1. There were no significant differences between patients and controls for age, gender, body mass index, heart rate, blood pressure, LV dimensions, and LVEF. As expected, LA dimensions ($P < 0.0001$, for all) and volumes (Vp, Vmin, Vmax, and Vs; $P < 0.0001$, $P < 0.0001$, $P < 0.0001$, and $P = 0.001$, respectively) were greater in the MS patients

Table 1. Demographic and conventional echocardiographic characteristics of patients with mitral stenosis and control subjects.

Variables	MS patients (n = 30)	Control subjects (n = 30)	P value
Age (years)	41 ± 7.9	42 ± 6.4	0.43
Gender (F/M)	19/11	20/10	0.47
BMI (kg/m^2)	24.4 ± 4.2	25.4 ± 4.5	0.67
Heart rate (bpm)	83 ± 12	81 ± 11	0.66
Systolic BP (mmHg)	112 ± 14	108 ± 12	0.48
Diastolic BP (mmHg)	72 ± 9	68 ± 6	0.22
LV-EDD (mm)	46.2 ± 4.1	45.5 ± 5.1	0.46
LV-ESD (mm)	30.3 ± 3.5	29.6 ± 3.6	0.64
LV-EF Simpson's (%)	63.4 ± 3.9	65.5 ± 4.4	0.68
LV-EF Teicholz (%)	63.3 ± 4.6	64.5 ± 4.3	0.74
LAD-ML (mm)	50 ± 7.2	36.5 ± 3.8	**<0.0001**
LAD-SI (mm)	58.9 ± 6.5	40.5 ± 4	**<0.0001**
LAD-AP (mm)	47.4 ± 7.2	34.1 ± 3.7	**<0.0001**
LA-Vp (mL)	84.7 ± 22.3	31.6 ± 5.5	**<0.0001**
LA-Vmin (mL)	62 ± 18.7	18.8 ± 3.9	**<0.0001**
LA-Vmax (mL)	105.9 ± 32.6	50 ± 7.6	**<0.0001**
LA-Vs (mL)	44 ± 19.7	31.2 ± 5.5	**= 0.001**
LA-EI (%)	75 ± 31.5	172.1 ± 9.5	**<0.0001**
LA-EF (%)	41.1 ± 10.3	62.2 ± 5.6	**<0.0001**
LA-AEF (%)	26.6 ± 10.9	39.8 ± 5.1	**<0.0001**
LA-PEF (%)	18.7 ± 8	35.6 ± 7.4	**<0.0001**
AVTIL (cm/s)	8 ± 1.4	10.4 ± 1.1	**<0.0001**
AVTIS (cm/s)	7.9 ± 1.5	10.2 ± 1.2	**<0.0001**
EKG-PR (ms)	168.8 ± 19.6	157.8 ± 13.3	**=0.015**

MS: mitral stenosis; BMI: body mass index; BP: blood pressure; LV: left ventricle; EDD: end-diastolic dimension; ESD: end-systolic dimension; EF: ejection fraction; LAD: left atrial diameter; ML: mediolateral; SI: superior-inferior; AP: anterior-posterior; LA: left atrium; Vp: pre-atrial contraction volume; Vmin: minimal volume; Vmax: maximal volume; Vs: stroke volume; EI: expansion index; AEF: active emptying fraction; PEF: passive emptying fraction; AVTIL: velocity time integral of the A wave lateral region; and AVTIS: velocity time integral of the A wave septal region.

than in the healthy controls (Table 1). Thus, LAEI (75 ± 31.5% vs. 172.1 ± 9.5%, P < 0.0001), LAEF (41.1 ± 10.3% vs. 62.2 ± 5.6%, P < 0.0001), LAAEF (26.6 ± 10.9% vs. 39.8 ± 5.1%, P < 0.0001), LAPEF (18.7 ± 8% vs. 35.6 ± 7.4%, P < 0.0001), AVTIL (8 ± 1.4 cm/s vs. 10.4 ± 1.1 cm/s, P < 0.0001), and AVTIS (7.9 ± 1.5 cm/s vs. 10.2 ± 1.2 cm/s, P < 0.0001) were lower in those patients compared to the controls. The PR intervals were longer in the patients than in the controls (168.8 ± 19.6 ms vs. 157.8 ± 13.3 ms, P = 0.015), and within normal limits. The mean mitral valve area value was calculated as 1.4 ± 0.3 cm^2 in the patient group.

For the quantitative assessment of the regional LA function, 8 segments in the 4 LA walls were evaluated in the 3 periods, one by one, with S/Sr echocardiography. Regional S analysis demonstrated that the patients with MS had significantly reduced S values in all of the segments for all 3 periods compared with the control subjects (P < 0.0001, for all 3 periods in all of the segments) (Table 2). When compared with the control group, Sr values were also significantly impaired in most of the segments of the LA walls in the MS patients (Table 3). Specifically, there were significant differences in Sr values between the MS patients and the controls for the interatrial septum and lateral LA wall segments in all of the periods. However, no significant differences were observed in the Sr values for the inferior LA wall segments, except for the COP between the groups. Interestingly, there were significant differences in Sr values for all of the LA wall segments in the COP between the MS patients and the controls (P = 0.001 for the superior segment of the inferior wall, P < 0.0001 for the others segments) (Table 3). There were no significant differences between the patients and the controls with respect to velocity indices in most of the segments of the LA walls, except for peak systolic velocities in the mid (4.7 ± 2.1 cm/s vs. 6.3 ± 1.9 cm/s, P = 0.003) and superior segments (3.7 ± 1.7 cm/s vs. 4.9 ± 2 cm/s, P = 0.004), and early diastolic velocities in the superior segments (3.4 ± 2.2 cm/s vs. 5.1 ± 1.9 cm/s, P = 0.003) of the lateral wall (Table 4).

For the time to peak systolic S, T-CP and T-COP were significantly higher in the patients than in the controls in most of the segments (anterior, inferior, and lateral walls) (P < 0.05). Additionally, for all of the segments, there were no significant differences for T-RP between the MS patients and the controls (P > 0.05). Interestingly, there were no significant

Table 2. Left atrial myocardial longitudinal peak systolic strain values of patients with mitral stenosis and control subjects in the 3 periods.

Strain (%)		Lateral		IAS		Anterior		Inferior	
		Mid	Superior	Mid	Superior	Mid	Superior	Mid	Superior
CP	Ct	–26 ± 4.4	–24.1 ± 4.3	–27.4 ± 5.8	–26 ± 4.4	–24.3 ± 4.4	–22.3 ± 4.5	–22 ± 4.3	–20.2 ± 4.1
	Pt	–16.6 ± 2.2	–15.7 ± 2.6	–17.9 ± 2.5	–16.7 ± 2.2	–16.4 ± 6.5	–16.1 ± 6.6	–15.6 ± 7.7	–14.4 ± 3.7
	P	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
RP	Ct	64.5 ± 6.7	62.2 ± 6.8	65.3 ± 7.4	63.5 ± 7.9	61.8 ± 5.6	59.8 ± 5.4	59.5 ± 5.2	57.6 ± 4.9
	Pt	44.7 ± 11.1	45.3 ± 10.1	45.7 ± 10.8	44.1 ± 10.5	46.5 ± 11.5	46.3 ± 11.2	45.3 ± 11	44.6 ± 9.7
	P	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
COP	Ct	–45.6 ± 6.5	–43.3 ± 6.5	–48.3 ± 6.3	–45.7 ± 6.2	–43.7 ± 6.2	–41.5 ± 6	–41.3 ± 6	–39 ± 5.9
	Pt	–23.2 ± 8.4	–23.6 ± 9.8	–23 ± 9.8	–22.2 ± 8.7	–23.5 ± 9.8	–23.6 ± 0.2	–23.7 ± 9.9	–23.3 ± 9.8
	P	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

IAS: inter-atrial septum; CP: contractile period; RP: reservoir period; COP: conduit period; Ct: control; and Pt: patient.

Table 3. Left atrial myocardial longitudinal strain rate values of patients with mitral stenosis compared with control subjects in the 3 periods.

Strain rate (s^{-1})			Lateral		IAS		Anterior		Inferior	
			Mid	Superior	Mid	Superior	Mid	Superior	Mid	Superior
CP		Ct	–4.8 ± 0.7	–4.6 ± 0.8	–5.2 ± 0.7	–4.9 ± 0.8	–4.5 ± 0.7	–4.3 ± .07	–4.3 ± 0.7	–4 ± 0.7
		Pt	–3.9 ± 0.9	–4 ± 1.2	–4 ± 1	–3.9 ± 0.9	–4.1 ± 0.6	–4.1 ± 0.8	–4.1 ± 0.7	–4 ± 0.7
		P	**<0.0001**	**0.037**	**<0.0001**	**<0.0001**	**0.028**	0.346	0.424	0.807
RP	E	Ct	5.6 ± 1	5.4 ± 0.9	6 ± 0.9	5.7 ± 0.9	5.4 ± 0.8	5.1 ± 0.8	5 ± 0.8	4.8 ± 0.8
		Pt	4.9 ± 1	4.8 ± 1.1	4.9 ± 1.1	4.9 ± 1.1	4.9 ± 1	4.8 ± 1	4.8 ± 0.8	4.9 ± 0.8
		P	**0.012**	**0.018**	**<0.0001**	**0.002**	0.064	0.314	0.358	0.898
	L	Ct	6.1 ± 0.9	5.9 ± 0.8	6.5 ± 0.7	6.3 ± 0.8	5.9 ± 0.7	5.7 ± 1	5.6 ± 0.8	5.4 ± 0.8
		Pt	4.9 ± 1.3	4.8 ± 1.3	5 ± 1.3	4.9 ± 1.3	4.9 ± 1.3	4.9 ± 1.2	5 ± 1.1	5.1 ± 1
		P	**<0.0001**	**0.001**	**<0.0001**	**<0.0001**	**0.001**	**0.007**	0.089	0.281
COP		Ct	–7.7 ± 0.9	–7.4 ± 0.9	–8 ± 0.5	–7.7 ± 0.7	–7.3 ± 0.8	–7.1 ± 0.8	–6.9 ± 0.8	–6.5 ± 0.9
		Pt	–5.4 ± 1.5	–5.3 ± 1.6	–5.1 ± 2.1	–5.1 ± 1.9	–5.4 ± 1.5	–5.4 ± 1.3	–5.4 ± 1.3	–5.3 ± 1.4
		P	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**0.001**

IAS: inter-atrial septum; CP: contractile period; RP: reservoir period; E: early reservoir period; L: late reservoir period; COP: conduit period; Ct: control; and Pt: patient.

Table 4. Left atrial myocardial systolic, early diastolic, and late diastolic velocities of patients with mitral stenosis compared with control subjects.

Velocity (cm/s)		Lateral		IAS		Anterior		Inferior	
		Mid	Superior	Mid	Superior	Mid	Superior	Mid	Superior
Peak S	Ct	6.3 ± 1.9	4.9 ± 2	4.9 ± 1.1	3.8 ± 1.3	4.2 ± 1.3	4.2 ± 1.3	4.3 ± 1.1	3.5 ± 1.1
	Pt	4.7 ± 2.1	3.7 ± 1.7	4.9 ± 1.1	4 ± 1.2	4.9 ± 2.1	4.1 ± 1.9	4.8 ± 1.9	4 ± 1.9
	P	**0.003**	**0.004**	0.786	0.674	0.08	0.826	0.08	0.65
E-D	Ct	5.2 ± 1.7	5.1 ± 1.9	5.1 ± 1.4	3.8 ± 0.9	4.7 ± 1.9	4.3 ± 1.3	4.8 ± 1.9	3.5 ± 1.1
	Pt	4.7 ± 2.7	3.4 ± 2.2	4.6 ± 1.6	4.1 ± 2	4.7 ± 2.3	4.7 ± 2.5	5.7 ± 2.8	4.2 ± 2.2
	P	0.624	**0.003**	0.07	0.562	0.898	0.371	0.169	0.104
L-D	Ct	5.3 ± 1.7	4.5 ± 2.2	4.6 ± 1.2	3.4 ± 1	4.3 ± 1.1	4.3 ± 1.4	4.8 ± 1.3	3.6 ± 1.4
	Pt	4.9 ± 2.4	3.5 ± 2.3	4.8 ± 1.2	3.8 ± 1.8	4.9 ± 2.2	4.4 ± 2.4	4.8 ± 2.1	4.2 ± 1.8
	P	0.685	0.07	0.562	0.371	0.318	0.923	0.681	0.227

IAS: inter-atrial septum; Peak S: peak systolic velocity; E-D: early diastolic velocity; and L-D: late diastolic velocity.

differences for time to peak S in interatrial septum segments between the groups, for all 3 of the LA periods (P > 0.05) (Table 5). For all of the segments, time to peak Sr was significantly higher in the MS patients than in the controls (P < 0.05), except for the mid-septal segment (230 ± 120 ms vs. 200 ± 20 ms, P = 0.398), for all 3 of the LA periods (Table 6). For the time to peak S/Sr values, T-COP > T-RP (L > E, for time to Sr) > T-CP distribution was observed in the MS patients and the healthy subjects (Tables 5 and 6).

Intraobserver and interobserver variabilities were good for peak systolic S, peak Sr, time to peak S, and time to peak Sr (5.7%, 8.2%, 8.8%, and 9.6%, respectively) but worse for systolic, early diastolic, and late diastolic velocities (10%, 13.2%, and 12.4%, respectively). However, these values were within acceptable ranges.

Discussion

To the best of our knowledge, this is the first study evaluating the regional longitudinal S/Sr deformation indices in patients with MS in the 3 LA periods, one by one. The present study demonstrated that the LA longitudinal myocardial functions are impaired in patients with isolated rheumatic MS, for all 3 of the LA mechanical periods, by S/Sr echocardiography. We found that S indices significantly decreased in all segments of the LA walls for each period in MS patients compared to the healthy subjects. Moreover, Sr indices were significantly lower in most of the LA segments for all periods in MS patients compared to the controls. We did not find significant differences between the 2 groups for velocity values in the 3 periods, again. However, our study is the first to demonstrate prolonged time to peak S/Sr of the LA in each period rheumatic MS. Presumably, this condition could be an additional factor to the deterioration of the regional LA myocardial function in MS patients. Time to peak Sr was found to be significantly delayed in MS patients compared to the controls for all periods at all of the LA segments, except for the mid-septal segments. This finding suggests that time to peak Sr could be used for assessment of the duration of the mechanical LA cycle, one by one, in MS patients. For the time to peak S/Sr values T-COP > T-RP (L > E, for time to Sr) > T-CP distribution was observed in the MS patients and in the healthy subjects. This distribution may contribute to LA desynchronization. These data have a significant contribution to the literature for the use of the S/Sr technique for determination of the duration of LA

Table 5. Time to peak systolic strain in patients with mitral stenosis compared with control subjects for the 3 left atrial periods.

Time to peak strain (ms)		Lateral		IAS		Anterior		Inferior	
		Mid	Superior	Mid	Superior	Mid	Superior	Mid	Superior
T-CP	Ct	120 ± 20	100 ± 30	130 ± 20	120 ± 20	110 ± 20	110 ± 20	110 ± 30	110 ± 30
	Pt	160 ± 10	150 ± 10	150 ± 10	140 ± 90	150 ± 50	150 ± 80	150 ± 40	150 ± 30
	P	0.123	**0.002**	0.591	0.372	**0.001**	**<0.0001**	**<0.0001**	**<0.0001**
T-RP	Ct	470 ± 70	450 ± 80	490 ± 80	460 ± 70	450 ± 70	430 ± 70	430 ± 80	420 ± 80
	Pt	500 ± 140	490 ± 110	510 ± 110	480 ± 110	480 ± 80	470 ± 90	470 ± 90	460 ± 90
	P	0.478	0.362	0.687	0.759	0.483	0.256	0.284	0.376
T-COP	Ct	690 ± 70	650 ± 70	720 ± 40	700 ± 50	650 ± 90	640 ± 80	620 ± 90	600 ± 90
	Pt	750 ± 160	740 ± 160	750 ± 140	740 ± 130	710 ± 70	700 ± 80	710 ± 80	710 ± 80
	P	**0.023**	**0.002**	0.765	0.060	**0.024**	**0.004**	**0.001**	**<0.0001**

T: time; IAS: inter-atrial septum; CP: contractile period; RP: reservoir period; COP: conduit period; Ct: control; and Pt: patient.

Table 6. Time to peak strain rate in patients with mitral stenosis compared with the control subjects for the 3 left atrial periods.

Time to peak strain rate (ms)			Lateral		IAS		Anterior		Inferior	
			Mid	Superior	Mid	Superior	Mid	Superior	Mid	Superior
T-CP		Ct	110 ± 20	100 ± 20	110 ± 10	100 ± 20	110 ± 30	100 ± 30	150 ± 10	100 ± 30
		Pt	150 ± 10	150 ± 10	150 ± 10	150 ± 10	140 ± 30	150 ± 40	150 ± 40	150 ± 40
		P	**0.001**	**<0.0001**	**0.005**	**0.002**	**<0.0001**	**<0.0001**	**0.002**	**<0.0001**
T-RP	E	Ct	190 ± 30	180 ± 30	200 ± 20	180 ± 20	180 ± 40	170 ± 40	170 ± 40	170 ± 40
		Pt	250 ± 140	240 ± 120	230 ± 120	240 ± 15	240 ± 100	230 ± 100	240 ± 80	230 ± 80
		P	**0.003**	**0.003**	0.398	**0.014**	**0.001**	**0.001**	**<0.0001**	**<0.0001**
	L	Ct	280 ± 30	270 ± 30	300 ± 20	280 ± 30	280 ± 40	270 ± 40	270 ± 40	270 ± 40
		Pt	400 ± 200	390 ± 160	390 ± 170	380 ± 160	400 ± 130	380 ± 120	400 ± 130	390 ± 130
		P	**<0.0001**	**<0.0001**	**0.042**	**0.001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
T-COP		Ct	610 ± 40	590 ± 50	640 ± 30	600 ± 40	590 ± 70	580 ± 70	570 ± 70	570 ± 60
		Pt	710 ± 160	690 ± 150	710 ± 110	700 ± 120	690 ± 100	690 ± 80	690 ± 100	700 ± 100
		P	**0.001**	**0.001**	**0.014**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

T: time; IAS: inter-atrial septum; CP: contractile period; RP: reservoir period; E: early reservoir period; L: late reservoir period. COP: conduit period; Ct: control; and Pt: patient.

contractile functions. However, Thomas et al. have demonstrated that atrial contraction was delayed in patients with chronic atrial fibrillation (10). Similarly, Wangs et al. claimed that the impaired conductivity of the LA led to decreased total active atrial contractions and prolonged interatrial conduction (8).

In our study, we used 3 indices calculated from the volumes for assessment of the LA contractile, reservoir, and conduit functions (by LAAEF, LAEI, and LAPEF, respectively). These indices are analogous to the LA systolic and diastolic functions. The LA reservoir dysfunction, which reflects "diastolic" dysfunction of LA, is likely to occur before LA booster dysfunction, which represents "systolic" dysfunction of the LA (15). Our study showed that systolic and diastolic dysfunction occurred in MS patients by previously mentioned indices and S/Sr parameters. LA dimension and volume values with CE in our MS patient group were compatible with those of previous studies (16-18). Similar to traditional parameters, AVTIL and AVTIS showed reduced atrial contractility in MS (10). Hesse et al. demonstrated that TDI A wave velocity was reduced in atrial dysfunction and A-wave velocity correlated with the LA fractional area and volume change (19). In our study, AVTIL and AVTIS were lower in the patients than in the controls. These findings support LA dysfunction due to rheumatic MS in our study by CE.

Atrial S/Sr demonstrated that the longitudinal shortening and lengthening of the atrium are discordant with the ventricular longitudinal motion because the atrium fills during ventricular systole and empties during ventricular diastole (20). Sirbu et al. have demonstrated that normal values of the LA walls S/Sr and the S/Sr imaging are feasible and provide good intra- and interobserver variability for assessment of LA function in the healthy subjects. These indices are helpful for determination of early signs of LA dysfunction in the absence of other echocardiographic evidence of atrial abnormality (2). Wang et al. have demonstrated that S/Sr imaging enables noninvasive quantification of LA dysfunction

due to hypertension and paroxysmal atrial fibrillation. They suggested that LA peak systolic S (LA passive stretching during LV systole) could be used as an index of LA reservoir function (8). Inaba et al. revealed that follow-up research is needed to determine whether LA dysfunction (evaluated using Sr imaging) is a predictor for the occurrence of adverse cardiovascular events (e.g., atrial arrhythmias, thromboembolism, and stroke) (21).

The pathophysiological role of the mechanical (valvular) and myocardial factors in LA dysfunction due to rheumatic MS is controversial. The inflammatory process due to acute rheumatic fever could affect the myocardium to varying degrees. This condition causes myocyte necrosis, interstitial fibrosis, calcification, disorganization of the atrial muscle bundles, and atrial fibrosis (22). As a result of these changes, myocytes lose their normal contraction and relaxation functions. Lee et al. demonstrated that varying degrees of ultrastructural pathological alterations of LV muscle cells, involving the myofibrils, mitochondria, nuclei, and other elements of the sarcoplasm and membranes surrounding the myocardial cells in rheumatic MS were present. They showed that these ultrastructural pathological findings did not correlate with the severity of MS. Furthermore, they reported that pathological alterations of myocardial ultrastructure were related to the extent of myocardial involvement by the rheumatic process rather than being structural adaptations in response to the hemodynamic derangement (23). In another study, it has been demonstrated that mitral annular velocity measured by the TDI technique increased after percutaneous mitral commissurotomy and that significant improvement could be due to the improved function of the subvalvular apparatus and myocardial segments (24). These data have shown that the major cause of LV systolic dysfunction in MS was impaired myocardial contractile function and not the hemodynamic factors. According to the results of our study, we suggest that atrial inflammation and structural changes due to rheumatic carditis are responsible for LA functional impairment.

There were several limitations in this study. The most important limitation was that the Doppler derived S/Sr technique is angle-dependent. We attempted to overcome this problem by reaching high frame rates, by narrowing the image window, and centralizing the assessed image. The second limitation was the image quality and the artifacts. In order to overcome this obstacle, measurements were performed from the images taken at the end of the expirium and included a minimum of 3 cycles. Third, we did not perform an invasive study because invasive or histological studies in asymptomatic MS patients are not ethically acceptable. Our last limitation was that only longitudinal LA variables were reported. Doppler derived S/Sr can theoretically measure transverse deformation variables, but it might be difficult to track acoustic kernels associated with radial movement of the thin LA wall from the apical position.

In conclusion, this study has demonstrated that S/Sr echocardiography enables detection of impairment of the LA contractile, reservoir, and conduit functions, analogous to LA systolic and diastolic functions in patients with rheumatic MS. The low levels of S/Sr in all of the LA cycles would be a signal of atrial fibrosis and atrial myopathy due to rheumatic fever in MS patients. We suggest that a delayed deformation period might be an additional factor to the deterioration of regional and global LA myocardial functions in MS patients. In addition, we showed that it may be possible to detect the accurate and reliable determination of the early period of subclinical LA myocardial dysfunction by S/Sr indices by the velocity indices in patients with MS.

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