Quantitative assessment of the left atrial myocardial deformation in patients with chronic mitral regurgitation by strain and strain rate imaging: an observational study

Kronik mitral yetersizlikli hastalarda sol atriyal miyokardiyal deformasyonun gerilim (strain) ve gerilim hızı (strain rate) görüntüleme ile kantitatif olarak değerlendirilmesi: Gözlemsel bir çalışma

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ABSTRACT

Objective: We evaluated regional left atrial (LA) myocardial deformations by strain (S) and strain rate (SR) imaging during LA pump, reservoir, and conduit phases in patients with chronic rheumatic mitral regurgitation (MR).

Methods: This cross-sectional observational study included 42 patients with moderate-to-severe MR who had normal left ventricular (LV) function, and 36 healthy control subjects. Conventional echocardiographic data were used to calculate LV and LA dimensions, volumes and functional indices (LA ejection fraction, LA active and passive emptying fraction). Longitudinal S/SR indices of the mid and superior segments of LA walls were measured during the three LA phases. Student t-test, Mann-Whitney U test, Chi-square test and Bland-Altman analysis were used for statistical analysis.

Results: LV systolic functions were similar in the patient and control groups. LV diameters, LA diameters and LA volumes were greater in the patient group compared with the control group (p<0.05, p<0.001, and p<0.001). LA ejection fraction and LA active emptying fraction values were lower in the patient group than in the control group (56±7 vs. 63±5%, 33±9 vs. 40±4%, p<0.05 for both). During the three LA phases, longitudinal S/SR values were significantly lower in all the segments in the patient group compared with the control group (p<0.001 for S, p<0.001 and p<0.05 for SR).

Conclusion: Regional LA longitudinal myocardial deformations are observed to be impaired during all the mechanical phases in patients with moderate-to-severe MR. Volume overload, remodeling and rheumatic effects may be responsible for the LA myocardial dysfunction in these patients. (Anadolu Kardiyo Derg 2012; 12: 377-83)

Key words: Deformation, strain, strain rate, mitral regurgitation, left atrium
**Introduction**

Chronic mitral regurgitation (MR) causes increased left ventricular (LV) and left atrial (LA) preload. Due to preservation of LV ejection fraction (EF), most of the patients remain asymptomatic for many years. Compensation of regurgitant volume by LA enlargement plays an important role in the generation of MR symptoms. However, this vicious cycle leads to LV volume overload which eventually results in LV and LA dysfunction (1, 2). LA remodeling caused by MR is target organ damage (3). LA enlargement is an important risk factor for atrial fibrillation, undesired cardiovascular events, stroke, and sudden cardiac death (1, 2, 6, 7).

Unlike LV, the atrial walls have a unique contraction/relaxation cycle due to having longitudinal and circumferential muscle bundles arranged in a complex manner (8). Atrial mechanical cycle is consisted of three phases: reservoir phase (RP) during LV systole, conduit phase (CP) during early and mid-period of the ventricular diastole, and pump phase (PP) which enhance LV filling during late diastole (9-11). Although LA volumes assessed by conventional echocardiography provide information about the global function, it remains inadequate for the quantitative assessment of myocardial function separately during each of these phases. LA dysfunction in patients with atrial fibrillation and myocardial infarction has been shown with tissue Doppler imaging (TDI) (12, 13). However, angle dependence and loading conditions limit the use of TDI in MR. Strain (S) and strain rate (SR) imaging modalities, derived from color TDI, are less affected from loading conditions, adjacent segments and translational heart motion. S/SR imaging methods have been used in the assessment of LV function in many cardiovascular diseases (14-17). S/SR imaging derived from TDI has been validated by quantitative assessment of regional LA deformation in healthy subjects (10, 14). In a few studies, LA deformation has been shown to be affected in various etiologies. While Moustafa et al. (18) showed decreased LA global S/SR measurements in primary chronic MR patients, Borg et al. (19) reported increases in LA deformation indices in patients with degenerative MR.

However, LA deformation indices in rheumatic MR have not been evaluated according to LA three mechanical phases.

Therefore, in this study, we aimed to evaluate LA deformation by S/SR imaging during each of the three LA phases (pump, reservoir and conduit phases) in patients with chronic rheumatic MR.

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**Methods**

**Study design**

This study was designed as a cross-sectional observational study.

**Study population**

The study population consisted of 42 rheumatic moderate-to-severe MR patients (26 women and 16 men; mean age, 43±6.2 years) with normal LV systolic function (EF > 50%), and age- and gender-matched 36 normal subjects (22 women and 14 men; mean age, 41±7.3 years), who were admitted to cardiology outpatient clinic in Atatürk University Faculty of Medicine between September 2009 and December 2009. The candidates had normal echocardiographic evaluation. Patients with hypertension, diabetes mellitus, atrial fibrillation, atrioventricular conduction anomalies, valvular heart disease other than MR, history of ischemic heart disease or revascularization, history of valvular surgery, acute coronary syndromes, LV systolic dysfunction, segmental wall motion abnormalities, pericardial disease, other causes of MR (ischemic, degenerative or myxomatous), as well as patients whose LA had an inadequate imaging quality, were excluded from the study.

Written informed consent was obtained from each of the patients and the study was approved by the institutional review board.

**Two-dimensional and Doppler echocardiography**

All patients underwent an echocardiographic examination in left lateral position by a GE Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) device using a 3.5 MHz transducer. End-expiratory echocardiographic records were obtained from standard apical 4-chamber, 2-chamber, apical long-axis, and parasternal long-axis views during three cardiac cycles. The entire data were transferred to a workstation for further offline analysis (EchoPAC PC; GE Vingmed Ultrasound AS, Horten, Norway). Echocardiographic assessment and measurements were performed according to the recommendations of the American Society of Echocardiography (20). LV end-diastolic and end-systolic diameters, LA diameters and volumes were calculated from two-dimensional echocardiographic views. LVEF was also calculated by averaging the Simpson and Teicholz methods (10, 20). Transmitral flow velocity during early filling (E) velocity was obtained by pulsed wave Doppler in the apical 4-chamber view. TDI was used to measure mitral annular velocities. The early diastolic velocity (E') was obtained in both the mitral septal and lateral annulus. The mean of the lateral and
significant. Independent Student t-test or Mann-Whitney U test were used to compare the continuous variables. Categorical variables were evaluated by the Chi-square test. Interobserver and intraobserver agreements were assessed by Bland-Altman analysis and intraclass correlation coefficient (ICC).

**Results**

**Baseline measurements**

The baseline characteristics of the study population are summarized in Table 1. There was no significant difference between the groups with regard to age, sex, body mass index, blood pressure and heart rate. Patient group had significantly increased LV end-
diastolic and end-systolic diameters (for both p<0.05, respectively), whereas LVEF was comparable between the groups (p>0.05). Patient group had significantly increased LA diameters and volumes (p<0.001). While the conventional LA function parameters, namely LAAEF, LAEI and LAEF, were significantly lower in the patient group (p<0.05, p<0.001, and p<0.05, respectively), there was no significant difference between the two groups in terms of LAPEF (p>0.05). There was significant difference between the control group and MR patients in regarding E/E’ ratio (p=0.001) (Table 1). It was observed that the New York Heart Association (NYHA) score did not show any notable correlation with that of the strain parameters in the reservoir, conduit and pump period (r<0.25, p>0.05).

**Left atrial deformation measurements**

S and SR measurements for each of the three LA phases were obtained from a total of 624 segments in 78 subjects. The analysis of LA longitudinal S revealed that the patient group had significantly lower S values in both mid and superior segments of the walls during each mechanical phase, compared with the control group (p<0.001) (Table 2). When patient and control groups were compared for LA longitudinal SR measurements, we found that patients had significantly lower SR in both mid and superior segments of the walls during each mechanical phase, compared with the control group (superior segments of anterior and lateral walls in PP, p<0.05; superior segments of the inferior wall both in PP and early RP, p<0.05; and all other segments during all three phases, p<0.001) (Table 3).

Inter-observer and intra-observer agreement results for S measurements of PP, RP and CP were as follows: 11.6±4.2% / 10.2±3.8% (ICC: 0.89, 95% CI 0.81-0.96), 8.8±3.6% / 7.3±2.8% (ICC: 0.87, 95% CI 0.80-0.95), and 7.4±3.1% / 6.6±2.9% (ICC: 0.90, 95% CI 0.83-0.96), respectively; whereas same results for the SR mea-

<table>
<thead>
<tr>
<th>Left atrial myocardial longitudinal peak systolic strain parameters</th>
<th>Lateral</th>
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<td><strong>Superior</strong></td>
<td><strong>Mid</strong></td>
<td><strong>Superior</strong></td>
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Results are shown as mean±standard deviation

*Student t-test and Mann-Whitney U test
surements of CP, early RP, late RP and PP were as follows: 4.6±1.2% / 4.1±1.1% (ICC: 0.84, 95% CI 0.72-0.95), 12.2±2.4% / 14.1±3.7% (ICC: 0.79, 95% CI 0.70-0.88), 16.8±2.1% / 19.3±3.4% (ICC: 0.79, 95% CI 0.67-0.88), and 19.7±4.1% / 20.6±3.9% (ICC: 0.79, 95% CI 0.68-0.91), respectively.

Discussion

Our study results based on the quantitative S/SR imaging demonstrated that patients with chronic rheumatic MR had impaired regional longitudinal LA myocardial deformation during each mechanical phase. Conventional echocardiographic findings in patients with MR showed that LA dimensions and volumes were increased, and global function parameters such as LAAEF, LAEI, and LAEF were decreased. In S/SR imaging, patients with MR had lower S/SR values for the mid and superior segments of all walls during all three phases, compared with the control group. Conventional and quantitative echocardiographic findings in patients with MR suggest that volume overload, dimensional enlargement, remodeling and rheumatic effects may play a role in the myocardial dysfunction of LA.

The principal hemodynamic function of the LA is to regulate filling of LV throughout the RP, CP and PP. Approximately 42% of the stroke volume is stored by the reservoir function of LA (28). The peristaltic-like movement of LA contraction, which begins at the superior aspect near the pulmonary veins, may minimize the backward atrial regurgitation flowing to the pulmonary veins, while moving blood towards the mitral annulus and the LV (29). Evaluation of LA myocardial function with conventional echocardiographic methods is very difficult and complex due to the absence of appropriate objective methods. Parameters that significantly affect loading conditions such as LAAEF, LAPEF and LAEI, while providing general information about the function of LA, cannot provide quantitative data about segmental and regional myocardial function of LA (5, 9). TDI and TDI-derived S/SR imaging have been shown to be more specific than conventional echocardiographic markers in the assessment of regional and global LA function. Moreover, they have been shown to play a role in determining the early period of subclinical disease (30). Our results demonstrated a significant deterioration in the LA reservoir function which shows LA filling during LV systole, LA conduit function that mediates filling of LV during diastole, LA pump function which provides support to LV filling and LAEF in patients with MR. Increased LA volume and mechanical load as a result of chronic MR, contributes to the development of atrial fibrillation (5, 7, 31). Atrial fibrillation develops in 48% of MR patients receiving medical therapy within a follow-up of ten years. Increased LA volume and atrial fibrillation have been found to be associated with increased mortality and morbidity, including sudden cardiac death (2, 3, 6, 7, 32-34). Surgical treatment is recommended as a class II indication in cases of new onset atrial fibrillation with MR (35).

In their study, Moustafa et al. (18) showed that LA volume indices (except LAPEF) were impaired in relation to the degree of MR, patients with mild MR had comparable S/SR measurements relative to the control group, and the moderate-severe MR group had significantly lower S/SR values compared with the healthy subjects and mild MR patients. Moreover, in our study, there was no significant difference between the patient and control groups with regard to LAPEF, and our S/SR measure-

<table>
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<td>Mid</td>
<td>Superior</td>
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*Student t-test and Mann-Whitney U test
ments were consistent with moderate-severe MR patients in this study. Similarly, Shin et al. (28) showed that patients with MR had significantly lower LA S measurements when compared to healthy subjects. On the contrary, Borg et al. (19) reported increases in LA deformation indices in relation to the increases in LA volumes in patients with degenerative moderate-severe MR. In this study, it is concluded that increased LA volume causes higher atrial compliance, raised preload causes higher contractile function according to Starling’s law, and myocyte hypertrophy leads to increases in deformity indicators. However, in the summary section, it was interestingly put forward that despite the increases in indicators of LA deformation and contractile functions, LA contribution to LV filling was reduced. The results of our study with regard to LA volumes and functional indicators conform to those in this study, with the exception that our S/SR value was different. Borg et al.’s (19) study population is relatively older than ours. While Borg et al. (19) found the end systolic diameter not to be different from the control group; EF values were significantly higher than the control group. In our study, on the other hand, end systolic diameter values in patients were substantially higher than the control group whereas there were no differences in EF between these groups in our study. Therefore, all these causes are effective factors on the different outcomes of the results. The lower value of our S/SR can probably be related to the rheumatic character of MR in our study. In rheumatic heart disease, a previous rheumatic illness has been shown to play a contributing role in LA and LV dysfunctions (36-38). Cameli et al. (39) used a new technique of two-dimensional speckle tracking echocardiography which revealed that indicators of longitudinal LA deformation were increased in mild MR patients; however, they were decreased in moderate and severe MR patients. While the increase in mild MR patients was associated with the increase in LA compliance, the decrease in moderate and severe patients was correlated to chronic MR-related structural abnormalities such as myocyte hypertrophy, interstitial fibrosis, and reduced metalloproteinase secretion. At the end, they concluded that indicators of LA deformation could be used to identify LA functions during the early stage of asymptomatic MR.

Study limitations
The most important limitation of our study was the artificial effects and the implemented S/SR techniques such as seen in TDI and S/SR studies. However, minimizing the screen window in order to raise the resolution and positioning the heart wall parallel to the ultrasound waves, reduced these errors to a minimum. Second limitation of our study was the lack of confirmation of LA functions via invasive methods in asymptomatic MR patients, which could have been an unethical step. However, in LV studies, S/SR indicators have been shown to match with the results of invasive methods. Third, patients with AF were not included in the study because LA demonstrates an extra contribution to the myocardial dysfunction. Four, mild MR patients were excluded from the study. Final limitation was the small number of our study sample, which required dividing the patients into moderate and severe MR groups.

Conclusion
Patients with chronic rheumatic MR exhibit abnormal LA longitudinal myocardial functions during all three mechanical stages, which can be evaluated quantitatively by S/SR imaging. Moreover, S/SR imaging can also be used for the serial follow-up of quantitative LA deformation (S/SR) data in chronic rheumatic MR patients. Therefore, it can be helpful in evaluating the MR progress and establishing the right timing for surgery before occurrence of irreversible myocardial damage. However, further studies involving large case series and long-term patient follow-ups are required.

Conflict of interest: None declared.

Acknowledgments

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