Subclinical left ventricular systolic dysfunction in patients with mild-to-moderate rheumatic mitral stenosis and normal left ventricular ejection fraction: an observational study

Hafif orta derecede romatizmal mitral kapak darlığı ve normal sol ventrikül ejeksiyon fraksiyonu olan hastalarda subklinik sol ventrikül sistolik disfonksiyonu: Bir gözlemsel çalışma

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ABSTRACT

Objective: Mitral valve stenosis (MS) remains as an important cause of morbidity despite evolution in diagnosis and treatment. Generally, left ventricular (LV) systolic functions are well preserved in patients with MS. However, there are some studies showing impaired LV systolic functions in patients with pure MS. The purpose of this study was to evaluate subclinical LV systolic dysfunction in a cohort of isolated mild-to-moderate MS patients with normal LV ejection fraction (EF) by using tissue Doppler imaging (TDI) and velocity vector imaging (VVI) techniques.

Methods: Fifty patients with isolated mild-to-moderate MS (84% female, mean age 49.1±10.0 years) and 60 healthy subjects (76.7% female, mean age 49.1±10.5) were included in this cross-sectional observational study. Conventional echocardiography, TDI, strain (S) and strain rate (SRs) analysis were performed in all patients.

Results: Transmitral mean pressure gradient was 6.4±3.0 mmHg and mean mitral valve area was 1.45±0.36 cm^2 in patients with MS. Both longitudinal and circumferential S and SRs were significantly reduced in patients with MS ($p<0.001$). TDI-derived parameters myocardial acceleration during isovolumic contraction (IVA) and peak velocity during systolic ejection (Sa) were also significantly decreased in patients with isolated MS ($p<0.001$). LV ejection fraction (EF) was not correlated with deformation indices. Deformation parameters were not correlated with transmitral gradient or mitral valve area.

Conclusion: VVI-derived deformation parameters may identify subclinical systolic dysfunction in patients with isolated MS with normal EF. These findings may give way to optimal timing for mitral valve surgery. *(Anadolu Kardiyol Derg 2013; 13: 328-36)*

Key words: Left ventricle, systolic function, deformation imaging, mitral valve stenosis, velocity vector imaging

ÖZET

Amaç: Tanı ve tedavideki gelişmelere rağmen mitral kapak darlığı (MD) genç erişkinlerde morbiditenin önemli bir sebebidir. Genellikle, MD olan hastalarda sol ventrikül (SV) fonksiyonları iyi korunmuştur. Ancak bazı çalışmalarda saf MD olan hastalarda SV sistolik fonksiyonlarının bozulduğu gösterilmiştir. Bu çalışmanın amacı; izole hafif-orta MD olan, normal SV ejeksiyon fraksiyonlu hasta kohortunda doku Doppler görüntüleme (DDG) ve hız vektör görüntüleme (HVG) yöntemlerini kullanarak, bu hastalarda subklinik sol ventrikül sistolik disfonksiyon varlığını araştırmaktır.

Yöntemler: İzole hafif-orta MD olan 50 hasta (%84 kadın, ortalama yaş 49.1±10.0 yıl) ve 60 sağlıklı kişi (%76.7 kadın, ortalama yaş 49.1±10.5 yıl) gözlemsel kesitsel çalışmaya dahil edildi. Tüm hastalara konvansiyonel ekokardiyografi, DDG ve HVG ile strain (S) ve strain oranı (SR) analizi yapıldı.

Bulgular: MD olan hastalarda ortalama transmitral gradient 6.4±3.0 mmHg ve ortalama mitral kapak alanı 1.45±0.36 cm^2 olarak bulundu. MD olan hastalarda hem longitüdinal hem de sirkümferensiyal S ve SR değerleri belirgin olarak düşük bulundu ($p<0.001$). DDG ile elde edilen izovolümik akselerasyon (IVA) ve sistolik dalga hızı (Sa) da izole MD olan hastalarda düşük olarak ölçüldü ($p<0.001$). SV ejeksiyon fraksiyonu deformasyon indeksleri ile korelasyon göstermemekte idi. Deformasyon indeksleri transmitral gradiyent ya da mitral kapak alanı ile ilişkili değildi.

Sonuç: Normal ejeksiyon fraksiyonu olan izole MD olan hastalarda HVG ile elde edilen deformasyon parametreleri subklinik sistolik disfonksiyonu gösterebilir. Bu bulgular mitral kapak cerrahisi için optimal zamanlamanın belirlenmesinde faydalı olabilir. *(Anadolu Kardiyol Derg 2013; 13: 328-36)*

Anahtar kelimeler: Sol ventrikül, sistolik fonksiyon, deformasyon görüntüleme, mitral kapak darlığı, hız vektör görüntüleme

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Accepted Date/Kabul Tarihi: 29.11.2012 **Available Online Date/Çevrimiçi Yayın Tarihi:** 26.03.2013

doi:10.5152/akd.2013.100

Introduction

The most important sequel of acute rheumatic fever is MS in long-term (1). Rheumatic MS has been recognized for more than 300 years (2). MS remains as an important cause of morbidity despite evolution in diagnosis and treatment. About 25% of all patients with rheumatic heart disease have isolated MS, and 40% have combined MS and mitral regurgitation (MR). Isolated MS causes increase in left atrial (LA) pressure, LA enlargement, pulmonary hypertension (PH), right ventricular (RV) enlargement and dysfunction.

Generally, LV systolic function is well preserved in pure MS, unless there is a coexisting MR (3). However, there are some studies pointing out impaired LV systolic function in pure MS (4-7). Myocardial structural changes and hemodynamic factors may play a role in the impairment of LV systolic function. Extension of inflammation through adjacent myocardium may lead alterations in systolic functions (8). Chronic decrease in preload and increase in afterload are also responsible for impaired LV systolic function in isolated MS (5).

Conventional parameters are not able to demonstrate subclinical LV dysfunction in MS patients. Tissue Doppler imaging (TDI) and strain/strain rate (SRs) imaging (SRI) are novel techniques that have been shown to be reliable and accurate for evaluating global and regional ventricular functions (9,10). TDI is preload and afterload dependent, SRI is also affected by afterload changes but less-load dependent than conventional parameter (11-13). Velocity Vector Imaging (VVI) is a novel two-dimensional strain imaging technique, which provides more accurate data on regional cardiac functions and is angle-independent (14, 15). VVI has been introduced to be a reliable method for quantification of regional contractile dysfunction with the ability to detect subclinical cardiac systolic dysfunction (11, 16).

The purpose of this study was to evaluate subclinical LV systolic dysfunction in a cohort of isolated mild-to-moderate MS patients with normal LV EF by using TDI and VVI techniques.

Methods

Study design

An observational cross-sectional study.

Patient population

All patients were included between April 2008 and August 2010. The study population consisted of 50 patients (mean age 49.1±10.0 years, 84 % female) with isolated rheumatic mitral valve stenosis and 60 age and sex-matched control subjects (mean age 49.1±10.5 years, 76.7% female). Exclusion criteria were as follows: 1. LV EF 50%, 2. mitral regurgitation more than mild degree, 3. aortic regurgitation more than mild degree or aortic stenosis, 4. tricuspid stenosis, 5. clinical, echocardiographic or angiographic evidence of coronary artery disease (CAD), 6. hypertension, 7. diabetes mellitus, 8. atrioventricular conduction abnormalities, 9. severe calcification of mitral valve annulus, 10. clinical or laboratory evidence of active rheumatic disease, 11. low quality echocardiographic image for TDI and VVI analyses, 12. atrial fibrillation.

Study protocol was approved by local Ethics Committee of our institute and a detailed written informed consent was obtained from each patient. The study was accomplished according to the Declaration of Helsinki.

Echocardiographic evaluation

Patients underwent a complete clinical examination as well as transthoracic echocardiography using Siemens Sequoia C256 ultrasound machine (Siemens Medical Systems, Mountain View, CA, USA) with 2.5-3.5 MHz transducer. Left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum and posterior wall thickness were obtained from parasternal long-axis view using M-mode tracings (17). From apical four-chamber view, LV end-diastolic and end-systolic volumes (LVEDV and LVESV) and LV EF were calculated using modified Simpson's method (18). LA volume is routinely measured at the end of ventricular systole, when LA volume is maximal, and is indexed to body surface area (BSA). Mitral valve orifice area was measured by planimetry method using 2-dimensional short axis images and by pressure half-time method using mitral valve Doppler tracings (19) in the apical four-chamber view. Mean transmitral diastolic gradient is also calculated by Doppler study. The systolic pulmonary artery pressure was derived from the tricuspid regurgitant jet velocity by using modified Bernoulli equation (20). Inferior vena cava (IVC) diameter was measured from subcostal longitudinal images with combination of M-mode, approximately 2 cm distal to the right atrial junction. Measurement of IVC was performed on the M-mode echocardiogram, at the end of the expiration. RAP was predicted by using the IVC size and collapsibility index, which was recommended by American Society of Echocardiography (18).

Tissue Doppler measurements

In the two-dimensional, four-chamber views, a 5-mm sample volume was placed just apical to the medial and lateral mitral annulus, identified using pulsed-wave TDI. Settings were adjusted for a frame rate between 120 and 180 frame/sec, and a cineloop of three to five consecutive heartbeats were recorded. TDI-derived systolic indices; IVA which is defined as the ratio of isovolumic velocity (IVV) divided by the acceleration time, and peak velocity during systolic ejection (Sa) (cm/s) were measured from mitral annulus. Peak early (Ea) (cm/s) and late diastolic (Aa) (cm/s) mitral annular velocities were also analyzed (Fig. 1). The myocardial performance index (MPI) was calculated as the sum of isovolumetric contraction time (IVCT) and isovolumetric relaxation time (IVRT) divided by ejection time (ET). All the measurements were calculated from three consecutive cycles and the average of these measurements was recorded.

Velocity vector imaging

Apical four- two-chamber, apical long-axis and parasternal short axis views were recorded with a frame rate 70 to 100 frame/s, for the VVI analysis. This frame rate is recommended by the vendor to combine temporal resolution with an acceptable lateral definition, to enhance the feasibility of the tracking technique. Three cardiac cycles were digitally stored for offline analysis. The high frame rate, acoustic captured, gray-scale recorded images were analyzed using Syngo VVI (Siemens Medical Solutions, Mountain View, CA, USA) software (Fig. 2). After the endocardial border was defined manually by the user, the VVI software automatically tracks the endocardial border throughout the cardiac cycles. This results in velocity vectors displayed in two-dimensional plane through the cardiac cycle. Comparison of displaced speckles in relation to one another along the endocardial border strain (S) and strain rate (SR) data. The LV walls are divided into three segments (apical, mid and basal) according to 16 segment-LV model of American Society of Echocardiography by the Syngo VVI system (21). Strain (%) and SRs (1/s) are defined as the change in the relative distance between localized tracked trace points, combined with the difference in the relative displacement of tissue motion behind the tracked points. Strain was defined as the instantaneous local trace lengthening or shortening and SRs as the rate of lengthening or shortening (11). Timing of events was performed using pulsed wave Doppler tracings recorded from heart cycles with comparable R-R intervals. For each segment, longitudinal and circumferential deformation indices were measured. We analyzed deformation index, which was used by Marciniak et al. (22) before, calculated by dividing LV deformation indices by LVEDV and LVESV.

Reproducibility

Intra-observer and inter-observer variability for VVI measurements were assessed. For intra-observer variability, a sample of 10 VVI measurements was randomly selected and examined by the same observer in two different days. For inter-observer variability, a second observer blinded to the clinical information and to the results of the first observer's results, examined the same 10 measurements. Intra-class correlation coefficients for the same observer and different observers were calculated (23).

Statistical analysis

All statistical data were performed by using Statistical Package for the Social Sciences 11.0 (SPSS 11.0, Chicago, IL, USA) program. Descriptive statistics is presented as mean±SD for continuous variables and as numbers and percentages for categorical variables. Continuous variables were analyzed using independent samples T-test or the Mann-Whitney U test, and qualitative variables were analyzed using the Chi-square test and Fisher's exact test when the expected frequency was <5. For assessment of correlations between continuous variables, the Pearson analysis was used. The results were considered significant, when the p value was less than 0.05.

Results

Clinical characteristics and conventional echocardiographic data

The demographic and conventional echocardiographic characteristics of the patients and the control group are shown in Table 1. Age, gender and body mass index (BMI) indices were similar in control group and patients with MS. The LVESD and LVEDD were in normal ranges both in patients and control groups but MS patients had larger LVEDD (p=0.01). IVS and PW thickness values were similar in both groups (p>0.05). LVEDV was similar in both groups (p=0.84) whereas LVESV was greater in patients with MS (p=0.004). LVEF was in normal ranges in patients and the controls. However patients with MS had significantly lower EF (p<0.001) when compared to the control group. Transmitral mean pressure gradient was 6.4±3.0 mmHg and mean mitral valve area was 1.45±0.36 cm^2 in patients with MS. LA diameter and LA volume index, calculated by dividing LA volume to body surface area (BSA) were increased in MS patients, compared to the control group. Only one-third of control subjects (20 subjects) and 5 of the MS patients had no tricuspid regurgitation and for this reason we were unable to determine systolic pulmonary artery pressure (sPAP) in these patients. Rest of the control subjects had trace or mild tricuspid regurgitation. As expected, SPAP was higher in MS patients, compared to the controls (p<0.001) (Table 1).

Tissue Doppler imaging findings

LV Sa value was significantly decreased in patients with MS, when compared to control group (0.09±0.03 cm/s to 0.12±0.03 cm/s, p<0.001). IVA, which is known as a reliable and volume-independent predictor of systolic functions, was significantly reduced in MS patients compared to the controls (2.8±0.94m/s^2 to 4.21±1.11 m/s^2, p<0.001). Considering LV diastolic functions, Ea and Aa velocities were significantly impaired in MS patients (0.09±0.05m/s vs 0.17±0.05 m/s and 0.09±0.04 m/s vs 0.14±0.03 m/s p<0.001). MPI, which is a good predictor of both systolic and diastolic functions, was significantly increased (0.69±0.15 to 0.29±0.04, p<0.001) in patients with MS, supporting markedly impairment in LV functions (Table 2).

Velocity vector-derived strain imaging

Strain and SRs data were obtained and analyzed from all patients and controls. Five hundred twenty eight segments over 600 segments were analyzed for determining LV circumferential peak systolic S and SRs. Longitudinal peak systolic S and SR analysis were analyzed from base, mid and apical segments of LV in apical four-chamber, two-chamber, long-axis views. We analyzed 1423 segments over 1600 segments for longitudinal peak systolic S and SRs.

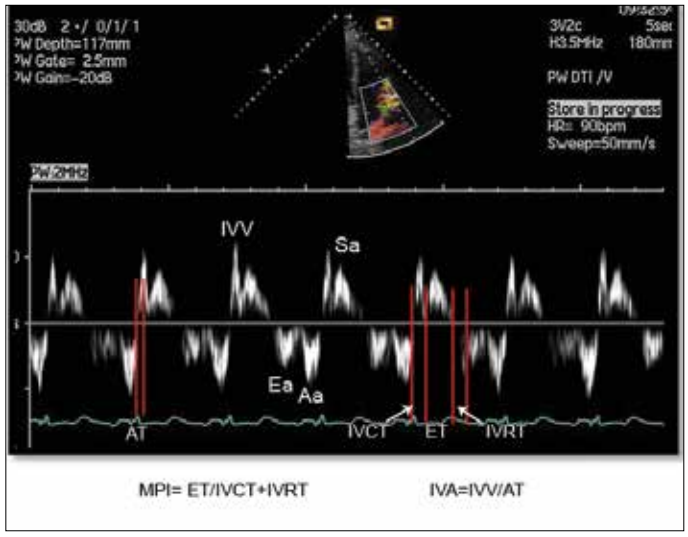

Figure 1. Measurements of tissue Doppler imaging (TDI) derived myocardial systolic velocities

Peak myocardial velocity during isovolumic contraction (IVV) (m/s); myocardial acceleration during isovolumic contraction (IVA) (m/s2), defined as the ratio of IVV divided by the acceleration time, peak velocity during systolic ejection (Sa)

AT - acceleration time; peak early, Aa - mitral annular velocities, Ea - late diastolic, ET - ejection time, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time

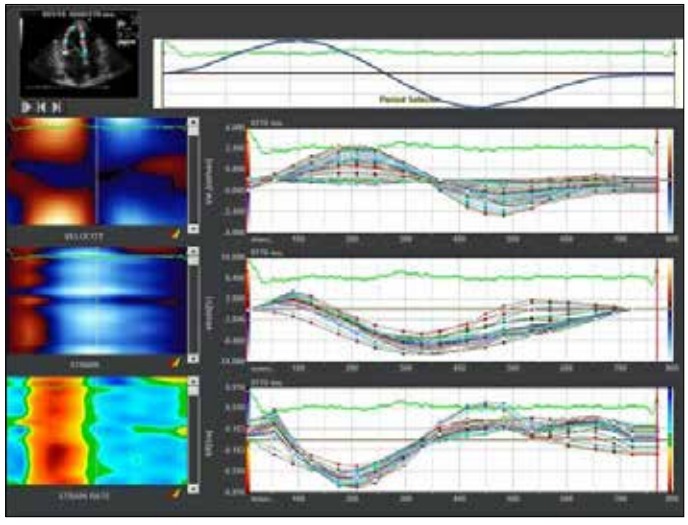

Figure 2. The color M-mode echocardiography map and time curves showing velocity, strain (%), and strain rates (1/s) in the apical four chamber view

LV Longitudinal peak systolic S and SRs were significantly decreased in MS patients in each segment compared to the control group (p<0.05) (Table 3). Mean strain values in inferior and inferior septum, mean strain rate values in inferior and inferior septum was lower than other walls. However, it was not statistically significant. The mean longitudinal peak systolic S and SRs were also significantly impaired in patients with MS, suggesting a global dysfunction rather than segmental dysfunction (p<0.001) (Fig. 3).

LV circumferential peak systolic S and SRs were significantly impaired in patients with MS for each segment compared to the control group (p<0.05) (Table 4, Fig. 3). LV circumferential peak systolic S and SRs values were also significantly lower in MS patients compared to controls (p<0.001) (Fig. 4).

Table 1. Demographic and echocardiographic features of patients with pure mitral stenosis and control subjects

Variables	MS patients (n=50)	Control subjects (n=60)	*p
Age, years	49.1±10.0	49.1±10.5	0.980
Female gender, n (%)	42 (84)	46 (76.7)	0.473
BMI, kg/m^2	27.4±4.1	26.3±5.4	0.224
LVEDD, cm	4.89±0.30	4.74±0.28	0.013
LVESD, cm	3.28±0.37	3.16±0.31	0.07
IVS thickness, cm	0.96±0.11	0.95±0.09	0.566
PW thickness, cm	0.93±0.11	0.95±0.11	0.463
LVEDV, mL	108.5±23.2	107.2±26.4	0.843
LVESV, mL	40.6±10.4	33.94±8.13	0.004
LVEF, %	61.0±4.7	66.6±4.1	<0.001
LAD, cm	4.89±0.59	3.60±0.19	<0.001
LAVI, mL/m^2	55.0±17.0	23.0±6.0	<0.001
MV E velocity, m/s	1.59±0.36	0.78±0.16	<0.001
MV A velocity, m/s	1.61±0.31	0.72±0.15	<0.001
sPAP, mmHg	38.1±10.0	22.0±6.0	<0.001
Trace TR, n (%)	15(30)	25 (41)	0.53
Mild TR, n (%)	30 (60)	35 (58.3)	

Data are presented as mean±SD, and number (percentage)
*Chi-square, independent samples t, Mann-Whitney U, and Fisher's exact tests
A - late atrial velocity, BMI - body mass index, E - early diastolic velocity, IVS - inter ventricular septum, LAD - left atrium diameter, LAVI - left atrium volume index, LVEDD - left ventricular end-diastolic diameter, LVESD - left ventricular end-systolic diameter, MS - mitral stenosis, MV - mitral valve, PW - posterior wall, sPAP - systolic pulmonary artery pressure, TR - tricuspid regurgitation

Table 2. Pulsed wave tissue Doppler measurements of left ventricle in patients in mitral stenosis and control subjects

Variables	MS patients (n=50)	Control Subjects (n=60)	*p
Peak Sa velocity, m/sn	0.09±0.03	0.12±0.03	<0.001
IVA, m/s^2	2.8±0.94	4.21±1.11	<0.001
LV Ea velocity, m/s	0.09±0.03	0.17±0.05	<0.001
LV Aa velocity, m/s	0.09±0.05	0.14±0.03	<0.001
LV Ea/Aa ratio	1.23±0.54	1.22±0.38	0.95
MPI	0.69±0.15	0.29±0.04	<0.001

Data are presented as mean±SD
*Independent samples t and Mann-Whitney U tests
Aa - peak late diastolic velocity, E - peak early diastolic velocity, IVA - isovolumic acceleration, LV - left ventricular, MPI - myocardial performance index, MS - mitral stenosis, Sa - peak systolic velocity

Correlation analyses

Correlation analyses for VVI-derived deformation indices among LV geometry parameters were performed. LVEDD was not

Table 3. Longitudinal peak systolic strain and strain rates of the each segments

Variables	MS patients (n=50)	Control subjects (n=60)	*p
İnferior septum basal strain, %	-15.50±6.12	-17.45±4.40	0.04
İnferior septum basal strain rate (1/s)	-0.75±0.24	-1.16±0.17	<0.001
İnferior septum mid strain, %	-15.29±5.35	-19.18±2.39	0.003
İnferior septum mid strain rate (1/s)	-0.75±0.34	-1.03±0.25	0.002
İnferior septum apical strain, %	-14.41±4.11	-19.02±4.15	<0.001
İnferior septum apical strain rate (1/s)	-0.71±0.21	-1.05±0.33	<0.001
Anterolateral basal strain, %	-16.35±5.72	-20.17±3.78	0.007
Anterolateral basal strain rate (1/s)	-0.88±0.31	-1.09±0.20	0.006
Anterolateral mid strain, %	-15.30±5.41	-19.13±3.05	0.004
Anterolateral mid strain rate (1/s)	-0.81±0.26	-1.07±0.08	<0.001
Anterolateral apical strain, %	-15.80±4.75	-17.06±1.08	0.048
Anterolateral apical strain rate (1/s)	-0.84±0.22	-0.97±0.05	0.01
Anterior basal strain, %	-17.59±5.86	-22.17±5.49	0.005
Anterior basal strain rate (1/s)	-0.92±0.38	-1.13±0.35	0.049
Anterior mid strain, %	-14.10±6.93	-21.48±5.15	<0.001
Anterior mid strain rate (1/s)	-0.90±0.44	-1.05±0.28	0.046
Anterior apical strain, %	-14.09±5.83	-18.95±4.66	0.002
Anterior apical strain rate (1/s)	-0.78±0.34	-1.02±0.28	0.008
İnferior basal strain, %	-13.35±5.70	-20.39±5.82	<0.001
İnferior basal strain rate (1/s)	-0.69±0.30	-1.13±0.39	<0.001
İnferior mid strain, %	-13.6±5.80	-19.83±3.85	<0.001
İnferior mid strain rate (1/s)	-0.68±0.41	-1.06±0.28	<0.001
İnferior apical strain, %	-14.16±5.32	-19.72±6.24	0.002
İnferior apical strain rate (1/s)	-0.75±0.31	-1.10±0.34	<0.001
Anterior septum basal strain, %	-12.83±5.72	-25.78±10.81	<0.001
Anterior septum basal strain rate (1/s)	-0.83±0.33	-1.55±0.98	<0.001
Anterior septum mid strain, %	-12.52±5.45	-24.31±8.96	<0.001
Anterior septum mid strain rate (1/s)	-0.76±0.24	-1.44±0.74	<0.001
Anterior septum apical strain, %	-13.29±4.92	-25.74±10.45	<0.001
Anterior septum apical strain rate (1/s)	-0.80±0.24	-1.49±0.80	<0.001
İnferolateral basal strain, %	-15.12±5.70	-18.98±3.65	0.008
İnferolateral basal strain rate (1/s)	-0.90±0.30	-1.05±0.19	0.049
İnferolateral mid strain, %	-15.24±5.08	-23.95±7.16	<0.001
İnferolateral mid strain rate (1/s)	-0.90±0.34	-1.48±0.62	<0.001
İnferolateral apical strain , %	-13.62±5.92	-21.34±5.53	<0.001
İnferolateral mid strain rate (1/s)	-0.83±0.32	-1.18±0.41	0.001

Data are presented as mean±SD
*Independent samples t -test
MS - mitral stenosis

correlated with LV longitudinal peak systolic strain and circumferential peak strain. There was a significant negative correlation between LVESD and LV longitudinal peak systolic S (r=-0.368, p=0.025) and we found statistically significant positive correlation between LVEF and LV longitudinal (r=0.428, p=0.016 for S and r=0.381, p=0.021 for SRs) and circumferential peak systolic strain (r=0.423, p=0.016 for S). There was no significant correlation between mean transmitral gradient and LV deformation indices. Additionally, we were not able to show a significant correlation between LV deformation parameters and mitral valve area.

Left ventricular deformation index analysis

We analyzed deformation index, and demonstrated a detailed analysis of deformation among LV geometry. We showed that LV longitudinal and circumferential deformation indices were significantly lower in MS patients when compared to the control group. (p<0.001) (Table 5).

Reproducibility

Intra-class correlations for intra-observer variability were good for VVI-derived parameters [longitudinal strain: 0.92, 95% confidence interval (CI) 0.76-0.97; circumferential strain: 0.90, 95% CI 0.77-0.98; longitudinal SR: 0.97, 95% CI 0.86-0.98; circumferential SR: 0.90, 95% CI 0.70-0.96]. The intra-class correlations for inter-observer variability were also good for VVI-derived measurements (longitudinal strain: 0.91, 95% CI 0.75-0.96; circumferential strain: 0.93, 95% CI 0.62-0.97; longitudinal SR: 0.94, 95% CI 0.77-0.98; circumferential SR: 0.91, 95% CI 0.73-0.98).

Discussion

Our study revealed subclinical LV systolic dysfunction in patients with mild-to-moderate rheumatic MS. We demonstrated that not only LV longitudinal deformation but also circumferential deformation was significantly impaired in these patients. We reported in our study that LV subclinical systolic dysfunction was independent from LV geometry, mitral valve area and mean transmitral gradient.

In patients with pure MS, varying degrees of LV systolic dysfunction may be observed (5, 6). Previous pathological studies demonstrated ultrastructural pathological alterations at different levels, independent from LV systolic function and the severity of MS (24). It has been reported in some studies that decreased preload, increased afterload and abnormal interventricular septal motion resulting from RV overload are responsible hemodynamic factors for decreased LV systolic performance. Sengupta et al. (25) suggested that in MS patients with impaired LV EF, early after percutaneous mitral comissurotomy, significant improvement was observed in LV tissue Doppler velocities. This improvement was significantly correlated with mitral valve area. However, there was no improvement in LV EF. According to these findings, it remains a challenge whether LV systolic deterioration is a result of functional or myocardial factors in patients with MS.

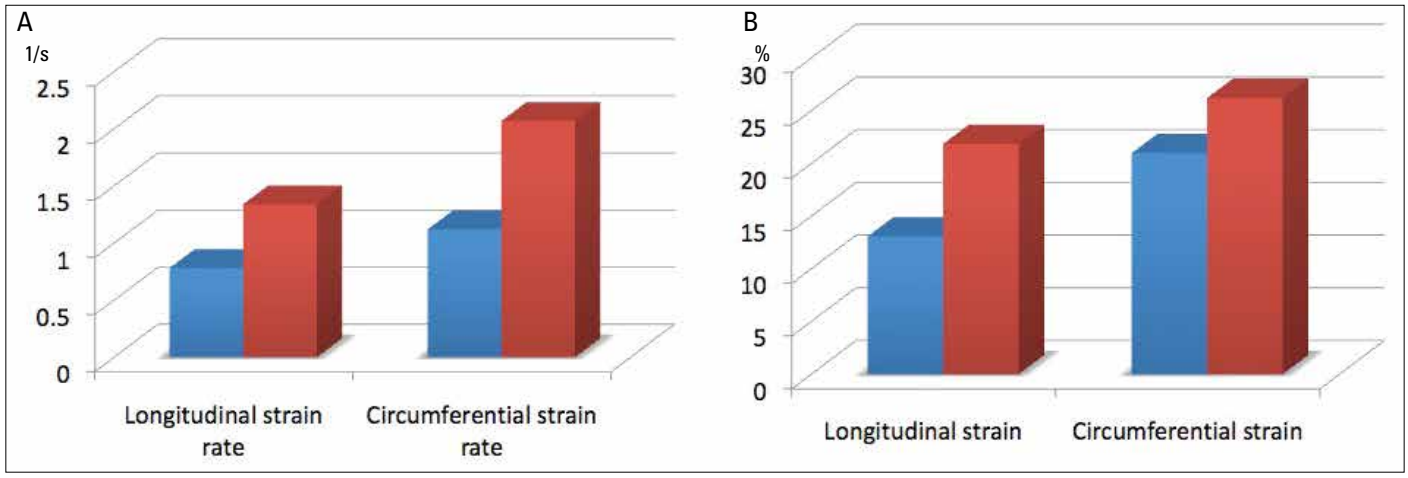

Figure 3. A) Mean longitudinal and circumferential strain rate values of the left ventricle, B) Mean longitudinal and circumferential strain values of the left ventricle

Table 4. Circumferential systolic strain and strain rates of the each segment at the middle layer in short-axis views

VVI Analyses	Patients	Inferior septum	Lateral	Anterior	Inferior	Anterior septum	Inferolateral
Strain, %	MS patients	-22.69±7.73¥	-18.80±7.65¥	-21.16±8.59	-21.20±8.38¥	-20.06±7.97	-19.30±7.65
	Control	-26.70±5.74¥	-22.59±6.79¥	-25.89±6.89	-25.20±5.27¥	-27.49±4.71	-23.95±4.73
Strain rate, 1/s	MS patients	-1.23±0.43	-1.06±0.40	-1.15±0.56	-1.13±0.53	-1.05±0.45	-1.11±0.56
	Control	-1.57±0.36	-1.39±0.37	-1.64±0.45	-1.49±0.28	-1.67±0.32	-1.47±0.30

Data are presented as mean±SD
Independent samples t -test - ¥: p< 0.05, p<0.001 for unmarked values
MS - mitral stenosis, VVI - velocity vector imaging

Table 5. Deformation index analysis of MS patients and control subjects

Variables	MS patients	Control Subjects	*p
Longitudinal deformation			
Strain/LVEDV	2.82±0.80	4.59±0.69	<0.0001
SR/LVEDV	0.16±0.04	0.28±0.06	<0.0001
Strain/LVESV	0.35±0.10	0.67±0.16	<0.0001
SR/LVESV	0.02±0.005	0.04±0.011	<0.0001
Circumferential deformation			
Strain/LVEDV	4.31±1.66	5.50±0.71	<0.0001
SR/LVEDV	0.22±0.09	0.43±0.11	<0.0001
Strain/LVESV	0.53±0.22	0.83±0.25	<0.0001
SR/LVESV	0.02±0.011	0.06±0.01	<0.0001

Data are presented as mean±SD
*Independent samples t -test
LVEDV - left ventricular end diastolic volume, LVESV - left ventricular end systolic volume, MS - mitral stenosis, SR- strain rate

LV EF is a widely used conventional parameter in evaluating LV global function in MS. However, it has an important limitation as not being able to detect subclinical LV systolic dysfunction. TDI-derived measurements also became widespread for quantifying global and segmental LV functions (26, 27). But it is angle and load dependent and has velocity aliasing limitation (28, 29). Currently, strain and SR imaging are considered as a superior method to conventional echocardiography and TDI, due to its ability to provide quantitative myocardial function analysis (30, 31). These recent parameters of systolic function are also affected by afterload changes but might be less load-dependent than conventional parameters (11, 32). The combined assessment of longitudinal and radial function of the left ventricle may be more sensitive and accurate in detecting subclinical changes in LV performance than conventional echocardiographic methods (33).

Previous studies revealed that MS patients with reduced global LV function usually demonstrated segmental contraction abnormalities (34). The tethering of posterobasal myocardium or restriction caused by scarred mitral apparatus has been implicated in segmental dysfunction of LV (35). In a recent study performed by Özdemir et al. (36) global and segmental LV dysfunction in MS patients was shown by using S and SRs imaging. They observed that S and SRs values were decreased especially in basal and mid segments of the LV. We found lower S and SRs values in anterior septum and inferior walls and especially in basal segments. In contrast to this study, Özdemir et al. (5) revealed LV global systolic and diastolic dysfunction in patients with pure MS using TDI. In another study, authors showed globally reduced LV long-axis function in MS patients with conventional parameters and TDI (6).

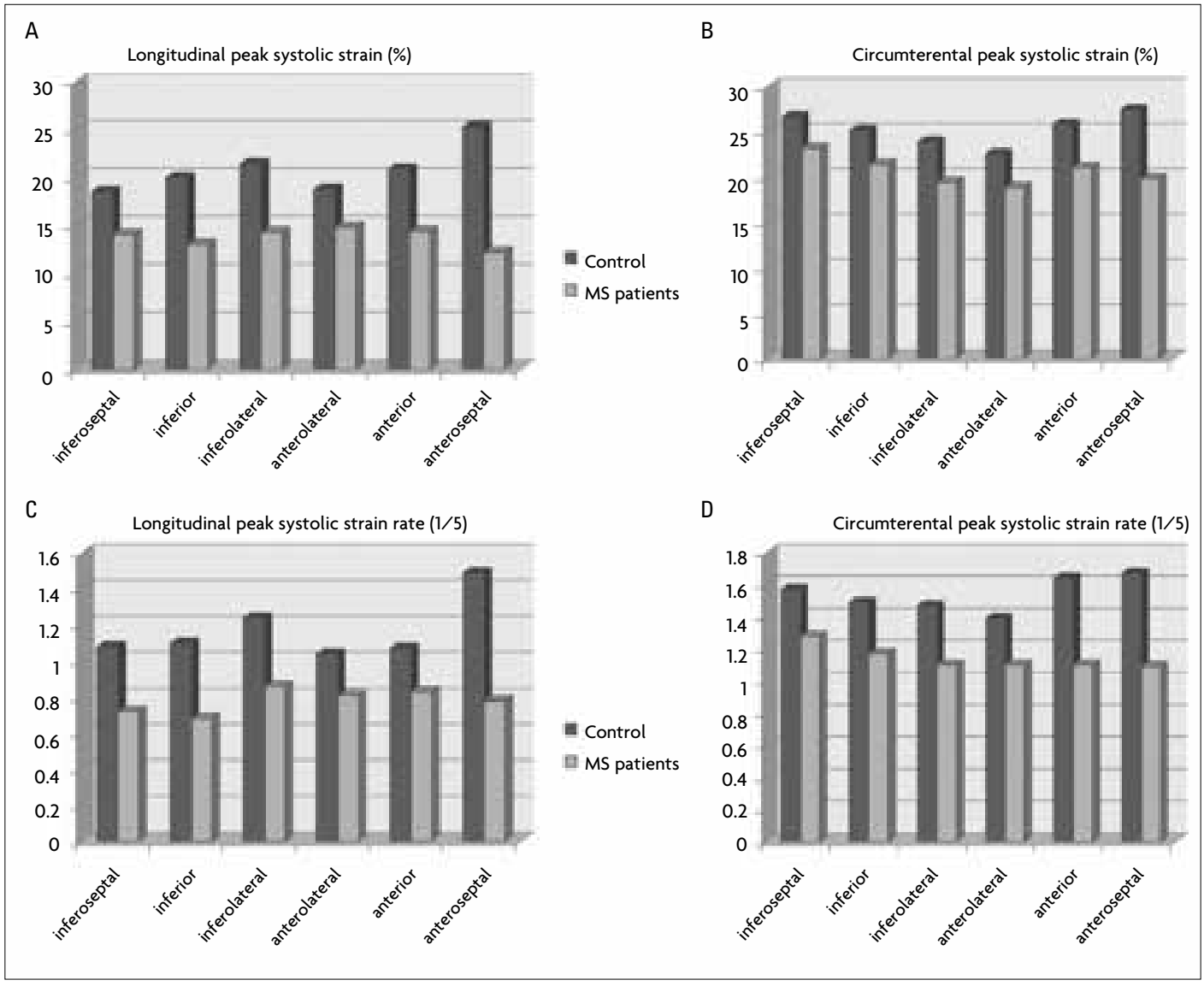

Figure 4. A) Segmental peak longitudinal strain of the left ventricle, B) Segmental peak longitudinal strain rate of the left ventricle, C) Segmental peak circumferential strain of the left ventricle, D) Segmental peak circumferential strain rate of the left ventricle

In this study, we used VVI-derived strain imaging to evaluate patients with pure MS. Despite preserved LV EF, we found significantly reduced longitudinal and circumferential systolic deformation in all LV segments. We also demonstrated that TDI-derived systolic indices (Sa and IVA) were significantly decreased in these patients, regardless of mitral valve area or mean transmitral gradient.

The fiber orientation of the heart is longitudinal in the subendocardial layer, and circumferential in the midwall of the heart (37). In our patients, longitudinal and circumferential deformation was found to be impaired, reflecting subclinical LV dysfunction. Decrease in LV myocardial performance is possibly caused by the inflammatory rheumatic process. Ultrastructural pathological alterations of myocardium in MS patients were shown in a study before. Lee et al. (24) revealed ultrastructural changes in myocytes, myofibrils, mitochondria, nuclei and other elements of the sarcoplasm and membranes in MS patients. Pathological alterations in the myocardial cells affected by rheumatic process may be responsible for impaired systolic performance, which may be consistent even after improvement in hemodynamics following valvuloplasty (34). It is suggested that LV systolic dysfunction in patients with pure MS is an end-point of the rheumatic changes in LV myocardium, rather than hemodynamic abnormalities.

Study limitations

We did not perform coronary angiography to our study population. All control subjects had negative exercise stress testing, but only 20 MS patients had stress testing. But we did not find any segmental wall motion abnormalities; therefore we assume that none of them had coronary artery disease. We also did not compare our results with golden standard modality like mag-

netic resonance imaging or sonomicrometry. Further studies needed to evaluate clinical and prognostic importance of LV subclinical dysfunction and role of this novel method in patients with MS.

Conclusion

VVI-derived strain imaging is a novel echocardiographic technique, which may be used as a reliable, non-invasive parameter for determining subclinical left ventricular dysfunction in patients with pure MS with normal LV EF. The results of our may give way to the optimal timing for mitral valve surgery in patients with preserved LV EF.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - Ö.Y., S.A.; Design - Ö.Y.; Supervision - F.F.H., Ö.Y., Y.T.; Resource - S.A., Ö.Y., S.Y.; Material - F.F.H., Y.T.; Data collection&/or Processing - F.F.H., Ö.Y.; Analysis &/or interpretation - S.Y., Ö.Y.; Literature search - Ö.Y., F.F.H.; Writing - Ö.Y.; Critical review - S.A., S.Y., Y.T.

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