Evaluation of torsion and twist mechanics of the left ventricle in patients with systemic lupus erythematosus

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Abstract

Objective: Myocardial involvement in systemic lupus erythematosus (SLE) has great importance. The aim of this study is to evaluate the rotation and twisting mechanics of the left ventricle (LV) in patients with SLE.

Methods: Forty-three patients fulfilled at least four of the American College of Rheumatology criteria for SLE and 30 individuals as controls were included in the study. SLE disease activity was assessed using the SELENA–SLEDAI score. Echocardiography was performed for all subjects. The patients fulfilled at least four of the American College of Rheumatology criteria for SLE were enrolled in the study. SLE disease activity was assessed using the SELENA-SLEDAI score. Echocardiography was performed for all individuals.Comparisons between groups were made using independent samples t-test with the standard statistical software (SPSS, version 15.0; SPSS Inc., Chicago, IL, USA). Each image was digitally stored for offline analysis. Measurement of global strain assessed by 17-segment model and rotational parameters were performed. LV ejection fraction was calculated by the biplane Simpson's method. Comparisons between groups were made using the independent samples t-test with the standard statistical software. A p value of 0.05 was considered statistically significant.

Results: The values of mean global longitudinal strain, basal global circumferential strain (GCS), mean basal radial strain, and apical GCS were significantly lower in SLE patients. The difference between basal rotation, apical rotation, twist of the LV, and torsion of the LV in the SLE patients and controls were not significant (8.8±5.5 vs. 10.6±5.8, p=0.183;-4.7±3.0 vs. -4.8±3.2, p=0.947; 11.7±6.4 vs. 13.2±6.4, p=0.366; and 1.8±0.8 vs. 1.9±2.3, p=0.725, respectively). Although there was not any significant relationship between SELENA–SLEDAI score and myocardial strain analyses of the LV, the basal rotation and the torsion of the LV were lower in patients with SLE having a SLEDAI score of ≥17 (p=0.024 for basal rotation and p=0.032 for torsion).

Conclusion: The number of segmental and global strain analyses were decreased in SLE patients with globally normal LVEF. The twist and torsion mechanics of the LV were preserved according to the control group, and the left ventricular torsion and basal rotation were found to be significantly decreased in those with an activity score of ≥17. *(Anatol J Cardiol 2016; 16: 434-9)*

Keywords: systemic lupus erythematosus, echocardiography, left ventricular mechanics, strain, torsion, and twist

Introduction

The prevalence of cardiac involvement in systemic lupus erythematosus (SLE) was reported to be upto >50%; therefore, cardiovascular disease has been acknowledged as a primary cause of morbidity and mortality in SLE (1). The increased risk of cardiovascular disease in SLE was first recognized in 1976 by Urowitz et al. (2) who described a bimodal pattern of mortality in their Toronto SLE cohort. The bimodal distribution of mortality risk factors in lupus is an "early" peak in mortality caused by disease activity and severity itself, whereas a "late" peak is related to cardiovascular diseases.

Although cardiac manifestations are often mild, myocarditis is the most characteristic feature of myocardial involvement. It has been reported that segmental areas of hypokinesis can be indicative for the disease; however, large echo series have found frequencies of global hypokinesis between 5% and 20% (3). The individuals are usually asymptomatic.

Assessment of the left ventricle (LV) rotation may provide important insights into different types of myocardial dysfunction. Left ventricular twist plays a pivotal role in the mechanical efficiency of the heart, making it possible that only 15% fiber shortening results in a 60% reduction in left ventricular volume (4). Left ventricular torsion, defined as the wringing motion of the heart as the apex rotates with respect to the base around the LV long-axis, plays an important role in LV ejection and filling (5).

Because subclinical features are more prevalent than clinically apparent disease, they can only be recognized by

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echocardiography and other non-invasive tests (6). Therefore, we sought to evaluate the rotation and twisting of the LV if the LV ejection and filling was affected because of segmental or global hypokinesis in asymptomatic patients with SLE.

Methods

Study design

Fourty three patients fulfilled at least four of the American College of Rheumatology criteria for SLE (7) and demographic and clinical properties matched 30 control subjects were enrolled in the study. None of the individuals had diabetes. SLE disease activity was assessed using the SELENA-SLEDAI score (8, 9). Echocardiography was performed for all individuals. Comparisons between groups were made using independent samples t-test with the standard statistical software (SPSS, version 15.0; SPSS Inc., Chicago, IL, USA). The study was approved by the Local Ethical Committee at our institution.

Study population

Forty-three asymptomatic patients with SLE and 30 individuals as controls according to their demographic and clinically properties such as age, gender, hypertension (HT), or smoking were enrolled in the study. Extensive screening for coronary artery disease was undertaken in all cases. Exercise stress test or myocardial perfusion scintigraphy were performed for the patients. Patients with known coronary artery disease or symptoms of angina, positive exercise stress test, left bundle branch block in ECG, arrhythmia, pericarditis, pulmonary hypertension, congestive heart failure, stroke, renal failure, and peripheral arterial disease were excluded. None of them had diabetes. We also excluded the patients with other forms of autoimmune diseases.

Echocardiography

The base and apex of the LV rotate in opposite directions. The term torsion is used for defining the base-to-apex gradient in the rotation angle along the longitudinal axis of the LV, expressed in degrees per centimeter or radians per meter. The absolute apex-to-base difference in LV rotation (also in degrees or radians) is stated as the net LV torsion angle. (10). The LV comprises obliquely oriented muscle fibers that vary from a smaller radius, right-handed helix at the subendocardium to a larger-radius, left-handed helix at the subepicardium. Systolic twisting deformation resulting from clockwise basal rotation and counterclockwise apical rotation as seen from the apex is the functional consequence of this three-dimensional helical structure.

Two-dimensional grayscale harmonic images at a frame rate of 60–80 frames/s were obtained in the left lateral decubitus position using a commercially available system (Vivid 7; GE, Horten, Norway). For each view, three consecutive cardiac cycles were acquired during a breath hold and digitally stored on a magneto-optical disc for offline analysis. Measurement of global strain assessed by a 17-segment model and rotational parameters were performed using dedicated software (Echopac PC, version 10.0; GE Medical Systems). For the assessment of myocardial strain using speckle tracking echocardiography, endocardial borders were manually traced in end-systole, with the software automatically tracking myocardial deformation. If poor tracking occurred, endocardial borders were readjusted manually until satisfactory tracking was achieved. Strain curves for each segment (summed average strain) were recorded. These measurements were made at apical and basal levels of visualized LV walls. Longitudinal systolic strain was measured in 2- and 4-chamber views.

Parasternal short-axis images were obtained both at the basal left ventricular and at the apical level as circular as possible. Rotation was achieved automatically by the software. Counter clockwise rotation was marked as a positive value and clockwise rotation as a negative value when viewed from the LV apex. LV twist was defined as the net difference (in degrees) of apical and basal rotations at isochronal time points and was automatically computed by the software from the values of the basal and apical rotation. LV torsion was then calculated as the ratio between LV twist (in degrees) and the LV diastolic longitudinal length (in cm) between the LV apex and the mitral plane. Aortic valve opening and closure timing was obtained by a pulsed wave Doppler tracing. LV ejection fraction was calculated by the biplane Simpson's method according to the recommendations of the ASE (11). Peak systolic velocity (Sm) was obtained from the septal and lateral sides of the mitral annulus in the four-chamber view with appropriate TDI settings.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences version 15.0 software for Windows (Chicago, IL, USA). Categorical data are expressed as frequencies. Continuous variables were presented as mean±standard deviation. x^2 test was applied to compare the influence of the categorical variables. Continuous variables were analyzed with Kolmogorov–Smirnov for testing normal distribution. Comparisons between groups were made using the independent samples t-test. To analyze independent predictors, linear regression analyses were used. Intraobserver reproducibility was analyzed using Spearman's correlation analysis.

Results

Of the 43 patients enrolled in this study, five were males (11%). We planned a study with 43 experimental subjects and 30 control subjects to reject the null hypothesis that the population means of the experimental and control groups were equal with a probability (power) 0.93. The Type I error probability associated with this test of this null hypothesis was 0.05.

Table 1. Demographic properties and clinical characteristics of both the SLE patients and the control group

	SLE patients (n=43)	Control group (n=30)	*P*
Age, years	35.7±13.7	36.6±9.7	0.777
Gender, n	8 male (18%)	7 male (23%)	0.628
HT, n	5 (11%)	2 (6%)	0.334
Weight, kg	70±11	74±11	0.431
Height, cm	163±8.0	164±7.8	0.104
LDL, mg/dL	122±30	125±35	0.728
Smoking, n	10 (23%)	6 (20%)	0.745
LVd, cm	4.7±0.5	4.5±0.3	0.196
LVs, cm	2.7±0.3	2.5±0.3	0.128
LV length, cm	7.3±0.6	7.2±0.7	0.437
LVED volume, mL	93.8±20.7	91.6±20.8	0.659
LVEF	60.9±10	64.7±5.5	0.073
E	82±18	91±13	0.030
A	73±17	71±14	0.479
E/e'	13±4.3	11±3.6	0.025
Sm lateral	9.4±2.0	12±2.2	0.000

EF - ejection fraction; HT - hypertension; LVd - left ventricle diastolic diameter; LVED - left ventricle end diastolic; LVs - left ventricle systolic diameter; n - number; SLE - systemic lupus erythematosus; Sm - peak velocity in systole.
• Comparisons between groups were made using the independent samples t-test with the standard statistical software (SPSS, version 15.0; SPSS Inc., Chicago, IL, USA). Categorical data are expressed as frequencies. A p value of 0.05 was considered statistically significant.

Table 3. The difference between basal rotation, apical rotation, twist and torsion of the left ventricle in SLE patient group and the control group

	SLE patients (n=43) (Mean ± SD)	Control group (n=30) (Mean ± SD)	*P*
Apical rotation, degree	8.8±5.5	10.6±5.8	0.183
Basal rotation, degree	-4.7±3.0	-4.8±3.2	0.947
Twist, degree	11.7±6.4	13.2±6.4	0.366
Torsion, degree/cm	1.8±0.8	1.9±2.3	0.725

n - number; SD - standard deviation; SLE - systemic lupus erythematosus.
• Comparisons between groups were made using independent samples t-test with the standard statistical software (SPSS, version 15.0; SPSS Inc., Chicago, IL, USA). A p value of 0.05 was considered statistically significant.

There were no significant differences in terms of age, gender, hypertension (HT), or smoking between the groups, and none of the individuals had diabetes. Demographic properties and clinical characteristics of both the SLE patients and the controls are shown in Table 1. Absolute values of mean global longitudinal strain (GLS), basal global circumferential strain (GCS), mean basal radial strain (RS), and apical GCS were significantly lower in SLE patients than in patients with normal myocardium in the control group (-20.0±3.0 vs. -22.4±3.1, p=0.002; -15.3±5.1 vs.-20.3±3.6, p<0.001; 40.7±19.4 vs. 51.5±15.8, p=0.015; -25.0±7.8 vs. -28.8±5.5, p=0.030, respectively). Myocardial segments were evaluated and anterior, anterosep-

Table 2. Evaluation of the myocardial segments of both the SLE patient group and the control group.

Circumferential strain % (Basal)	SLE patients (n=43) (Mean±SD)	Control group (n=30) (Mean±SD)	*P*
Anterior	-17.9±6.5	-23.3±6.2	0.001
Anteroseptum	-20.7±7.9	-26.5±4.8	0.001
Inferior	-13.1±6.9	-17.0±6.5	0.021
Posterior	-11.5±6.3	-13.5±6.8	0.220
Lateral	-14.3±5.4	-16.8±6.2	0.083
Septum	-19.9±7.8	-24.3±7.5	0.019
Global	-15.3±5.1	-20.3±3.6	<0.001
Mean radial strain	40.7±19.4	51.5±15.8	0.015
Circumferential strain % (apical)			
Anterior	-25.7±8.3	-31.6±7.9	0.005
Anteroseptum	-25.5±7.9	-29. 0±6.0	0.046
Inferior	-24.3±7.9	-27.0±6.0	0.126
Posterior	-23.9±8.5	-27.7±7.1	0.062
Lateral	-24.7±7.8	-29.8±5.6	0.011
Septum	-24.7±7.8	-27.0±5.6	0.191
Global	-25.0±7.8	-28.8±5.5	0.030
Mean radial strain	27.9±15.1	34.4±13.5	0.074
Longitudinal strain %	**SLE patients (n=43) (Mean±SD)**	**Control group (n=30) (Mean±SD)**	***P***
Basal septum	-5.8±0.6	-6.7±1.1	<0.001
Mid-septum	-3.8±0.5	-4.4±0.7	<0.001
Apikal septum	-1.9±0.7	-2.0±0.7	0.510
Apikal lateral	-2.7±1.1	-3.0±1.1	0.350
Mid-lateral	-4.4±1.6	-5.3±1.5	0.021
Bazal lateral	-6.0±1.6	-6.9±1.4	0.017
Bazal inferior	-6.7±0.9	-7.4±1.5	0.046
Mid-inferior	-4.4±0.9	-4.9±0.9	0.066
Apikal inferior	-2.2±0.8	-2.1±0.5	0.628
Apikal anterior	-2.2±1.2	-2.2±0.7	0.961
Mid-anterior	-3.5±1.2	-4.2±1.3	0.065
Bazal anterior	-5.5±1.2	-6.3±1.5	0.022
Global LS	-20.0±3.0	-22.4±3.1	0.002
Sm Lateral	9.4±2.0	12.3±2.2	<0.001
Sm Septal	8.1±1.3	10.4±1.4	<0.001

LS - longitudinal strain; n - number; SD - standard deviation; SLE - systemic lupus erythematosus; Sm - peak velocity in systole
•Comparisons between groups were made using the independent samples t-test with the standard statistical software (SPSS, version 15.0;). A p value of 0.05 was considered statistically significant.

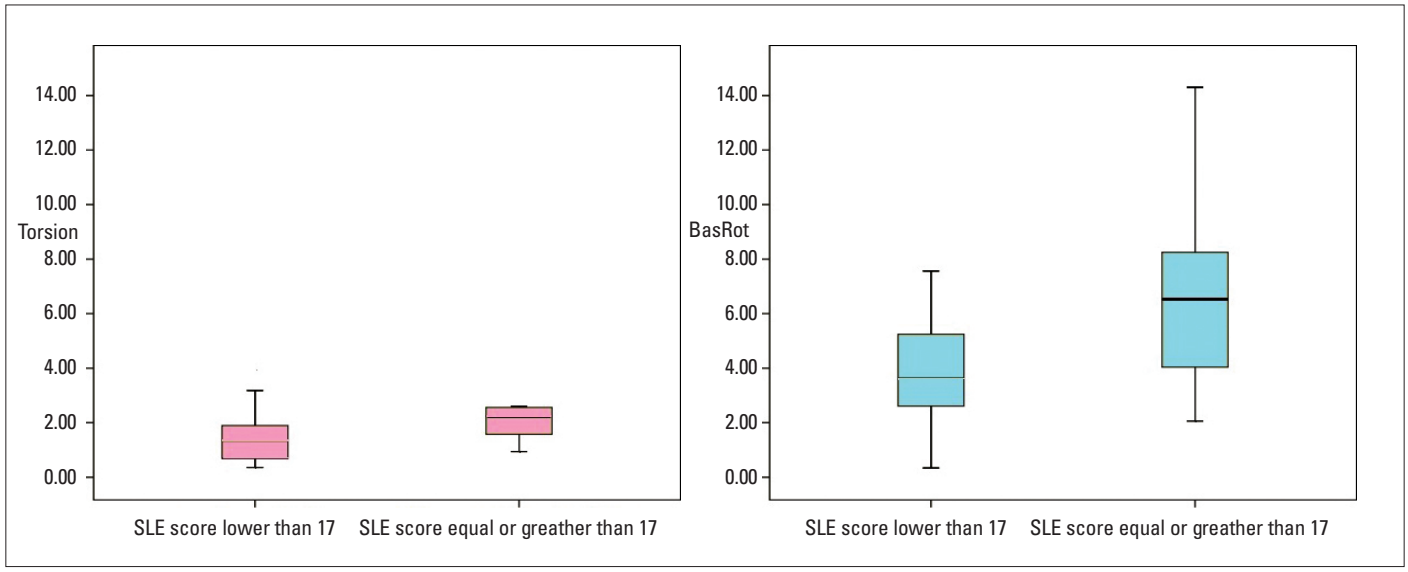

Figure 1. This figure shows significant differences in basal rotation and the torsion of the left ventricle between the patients with SELENA–SLEDAI scores of <17 and ≥17 (p=0.024 for basal rotation and p=0.032 for the torsion of the left ventricle)

The independent samples t-test

tum, septum, and inferior segments by basal circumferential strain (CS), anterior, anteroseptum, and lateral segments by apical CS, basal septum, mid-septum, basal lateral, mid-lateral and basal anterior segments by LS analyses found significantly depressed. Also, Sm lateral and Sm septal were found to be significantly lower in the SLE group by tissue Doppler echocardiography (9.4±2.0 vs. 12.3±2.2; p<0.001 and 8.1±1.3 vs. 10.4±1.4; p<0.001, respectively) (Table 2).

The difference between basal rotation, apical rotation, twist of the LV, and torsion of the LC in SLE patients and controls were not significant (8.8±5.5 vs. 10.6±5.8, p=0.183; -4.7±3.0 vs. -4.8±3.2, p=0.947; 11.7±6.4 vs. 13.2±6.4, p=0.366; 1.8±0.8 vs. 1.9±2.3, p=0.725, respectively, Table 3). However, there were significant differences in basal rotation and the torsion of the LV between the patients with a SELENA–SLEDAI score of <17and ≥17 (p=0.024 for basal rotation and p=0.032 for the torsion of the LV, Fig. 1). No significant relationship was found between SELENA–SLEDAI score and myocardial strain analyses of the LV in patients with SLE.

Intraobserver reproducibility was r=0.867, p<0.001.

Discussion

One of the most important point in our study is the values of the strain analyses; GLS, basal GCS, mean basal radial strain (RS), and apical GCS were significantly lower in SLE patients than in patients with normal myocardium in the control group by the two-dimensional speckle tracking imaging. However, Huang et al. (12) analyzed left ventricular global structure and systolic function in patients with SLE using the three-dimensional speckle tracking imaging and demonstrated that peak systolic GLS and GRS were significantly decreased in patients with severe SLE disease activity.

Cardiac rotation around the long-axis is an important component of LV systolic function and LV twist that is related to myocardial contractility and structure and has been recognized as a sensitive indicator of cardiac performance (13). Buss et al. (14) showed that SLE is associated with a significant impairment of systolic and diastolic LV longitudinal function in patients without cardiac symptoms. Nevertheless, Leal et al. (15) revealed subclinical systolic dysfunction even in the right ventricle in patients with childhood-onset SLE. It has been shown that systolic twist is maintained even in patients with anterior wall myocardial infarction but with relatively preserved LV systolic function (16, 17). Similarly, we found that the twist and torsion mechanics of the LV were preserved, despite the number of segmental and global strain analyses being decreased in patients with SLE as compared with those with globally normal left ventricular EF.

SLE may tend to predominantly cause subendocardial dysfunction that results in an early preferential involvement of longitudinal LV mechanics, which can be identified even in a subclinical state. The timing of contraction–relaxation cross-over is the most vulnerable period of myofiber mechanics (18, 19). Preserved LV torsion and twist mechanics may indicate that the ability of the LV to modulate the timing of contraction–relaxation cross-over is preserved in patients with globally normal LVEF, despite the impaired left ventricular segmental strain analysis in SLE. Although the twist mechanics of the LV were preserved according to the control group, the left ventricular torsion and basal rotation were found to be significantly decreased in those with an activity score of ≥17. The interplay of multiple inflammatory mediators, including leukocytes, cytokines, chemokines, adhesion molecules, complement, and antibodies may also result in the formation of cardiovascular diseases in the pathogenesis of SLE itself (20). Moreover, it has

already been suggested that SLE should be regarded as an equivalent to coronary heart disease, similar to diabetes (21).

Another important point in this study is that despite the preserved left ventricular twist mechanics according to the control group, the segmental and global strain analyses were found to be reduced, which may be an early indicator of the cardiovascular diseases before the symptoms begin in patients with SLE. This result may raise a question regarding SLE that whether the disease itself is enough to cause a cardiovascular disease such as diabetes in a patient depending on the disease activity assessed using the SELENA–SLEDAI score. We believe that these results in this study may indicate that the cardiac involvement is directly related to the risk score of the patients with SLE, and the left ventricular torsion and basal rotation decreases with an increasing activity score.

Despite the absence of symptoms, we believe that an ultimate goal of cardiovascular assessment to diagnose early cardiovascular disease is necessary, which will hopefully help us to prevent its progression. The evaluation of strain analysis and twist mechanics of the LV with two-dimensional speckle tracking echocardiography may be a useful technique and an important component of the cardiovascular assessment in patients with SLE.

Study limitations

We do not know the data regarding the patients with reduced left ventricular EF. Although male patients were included in this study, to completely understand the physiological principles of LV segmental strain and torsion mechanics and the future relationship between cardiovascular diseases and disease activity in patients with SLE, additional studies with large series and long-term follow-up are necessary.

Conclusion

The number of segmental and global strain analyses was decreased in SLE patients with globally normal LVEF. The twist and torsion mechanics of the LV were preserved, and the left ventricular torsion and basal rotation were significantly decreased in those with an activity score ≥17. The cardiovascular assessment to diagnose cardiovascular diseases early despite the absence of symptoms may help us to prevent its progression.

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