Left ventricular mechanics in Behcet's disease: A speckle tracking echocardiographic study

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Abstract

Although cardiac involvement is rarely seen in Behcet's disease (BD), it is essential to detect subclinical left ventricular (LV) dysfunction for prognostic purposes. Herein we aimed to show the role of two dimensional (2D) speckle tracking echocardiography (STE) in determination of subclinical LV dysfunction in patients with BD. 30 patients diagnosed as BD due to International Study Group Behcet's diagnostic criteria and 25 control subjects underwent Doppler echocardiography including pulsed tissue Doppler of the mitral annulus and speckle-tracking echocardiography. LV peak longitudinal strain and strain rate (SR) was calculated in four-chamber (4C), apical long-axis (LAX), and two-chamber (2C) views, and values of the three views were averaged LV global longitudinal strain (LV-GLS) and SR. LV torsion was determined as the net difference in the mean rotation between the apical and basal levels. There was not any significant difference in age and gender between groups. Patients with BD had significantly lower LV longitudinal strain and Sr measurements than the control group. Although LV basal rotation (LVR) basal values were similar in both groups, LVR-apical and LV torsion (LVTR) values were significantly higher in patient group. LVR-apical and LV-GLS were found to have a good positive corelation (r: 0.44, p<0.001) (r: -0.56, r: -0.65, respectively. p<0.001). There was a weak positive correlation between LVTR and LV-GLS (r: 0.29, p<0.05). We demonstrated that combined assessment of LV-GLS, LV-GLSR, LVTR and LVR-apical values detected by STE can be useful in determination of subclinical left ventricular dysfunction in BD.

KEY WORDS: Behcet's disease, speckle tracking echocardiography, torsion, rotation

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INTRODUCTION

Behcet's disease is a multisystemic, vasculitic, chronic disorder characterized by recurrent oral aftous lesions, iridocyclitis with hypopyon and genital ulcers. Skin, joint, central nervous, gastrointestinal, pulmonary and cardiovascular system involvement were reported in addition to the major findings of this disorder [1]. Cardiac involvement in BD is called as cardio-Behcet's disease [2]. Although the mean age of the onset of the BD is most commonly the third decade, the final diagnosis is usually made in the fourth decade [3]. The incidence and nature of cardiac involvement in BD are not yet clearly documented. Endocarditis, myocarditis, pericarditis, intracardiac thrombus, endomyocardial fibrosis, coronary arteritis, myocardial infarction and valvular disease are among the cardiac manifestations [4]. Endothelial dysfunction, left ventricular diastolic dysfunction, ventricular arrhythmias and sudden cardiac death were reported in some recent studies [5,6].

Incidence of arrhythmias and left ventricular diastolic dysfunction (LVDD) were found to be higher in BD patients [7,8]. Cardiac involvement in BD is rare, however the determination of subclinical LVDD is important in the prognosis of these patients. Tissue Doppler imaging (TDI) and Doppler strain have some limitations such as angle dependence, lower spatial resolution and deformation analysis in one dimension. On the contrary, 2D strain is a novel method performing strain measurements with standard two-dimensional echocardiographic images by speckle tracking, which is less angle dependent and more reproducible than conventional Doppler strain and TDI. Moreover studies about subclinical left ventricular (LV) myocardial deformation is insufficient in the literature, so we aimed in our study to show the effect of BD on subclinical LV

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myocardial deformation and diastolic function by 2D speckle tracking echocardiography (STE).

MATERIALS AND METHODS

Patients

The study group included 30 consecutive BD patients (20 male and 10 female) with a mean age ± SD of 28.5±7.1 years and 25 healthy volunteers from our hospital staff (16 male and 9 female) with a mean age of 27.8±4.9 years. The diagnosis of BD was made according to criteria of the International Study Group for Behcet's Disease [9]. Patients with coronary artery disease, hypertension, diabetes mellitus, obesity (BMI >30 kg/m^2), heart failure, cardiomyopathy, moderate to severe valvular disease, smoking, pulmonary disease, renal failure, hematologic disorder were excluded from the study. None of the patients had cardiac involvement or vascular complications. Patients had not received any topical or systemic treatments (e.g., steroid therapy) for at least 3 months before blood collection and echocardiographic evaluation. Disease activity was evaluated by physical manifestations, such as oral aphthous, genital ulcerations, uveitis, and vasculitis [10]. Patients with active disease manifestations during blood sampling were also excluded from the study. This study was conducted according to principles of the Declaration of Helsinki and approved by the local Ethics Committee. All of the patients were informed before the study and written consents were taken.

Standard Echocardiographic Evaluation

As described, echocardiographic evaluation was performed while the patients were in clinical remission in routine clinical controls according to the criteria of the American Society of Echocardiography [11]. None of the patients were under any cardiac medication during echocardiographic evaluation. All echocardiographic measurement were performed by two independent observers. Transthoracic examinations were performed by Vivid 7 Dimension® (GE Vingmed Ultrasound AS, Horten, Norway) echocardiography device using 2.5 MHz transducer. The patients were evaluated after 5 minutes of rest and in the left lateral decubitis position. At first, pericardium, valvular structures and wall motion were assessed by M mode and 2D echocardiography. Interventricular septal thickness, LV ejection fraction (LVEF), left atrial (LA) and aortic diameters were measured in the parasternal long axis. Pulse wave (PW) Doppler examination of LV filling was performed in apical fourth chamber using a sample volume parallel to the LV long axis at the mitral valve tip level and the average value of these measurements was taken. Mitral early diastolic flow velocity (E), late diastolic flow velocity (A) and deceleration time (DT) were recorded. PW Doppler sample volume with 5 mm width was adjusted at the intersection point of posterior wall and mitral annulus in apical four chamber view. Sample volume was provided to be parallel to the wall axis and peak early (Em), late (Am) diastolic flow velocities and LV peak systolic wave (S) velocities were measured. All of the measurements were repeated during three consequent heart beats and the mean of these measurements was taken.

Two-Dimensional Echocardiography

Two-dimensional speckle tracking analyses were performed on gray scale images of the LV obtained from the apical four- and two chamber views and parasternal long axis views. All images were obtained while the patients held their breath and the images were stored in a cineloop format from three consecutive beats. Then, the records were processed by acoustic tracking software (EchoPAC version 7.0, GE Vingmed). The frame rate was 60-90 frame/second. 16 segment LV model was derived from apical 4 and 2 chamber and parasternal long axis view records. After defining the endocardial border manually, tracing was performed by the software system automatically for each view. If the tracking was not satisfactory, manual adjustments were made at the tracking points throughout the cardiac cycle and thereafter automatic tracking repeated until satisfactory tracking results were achieved. Apical 4 chamber strain (LVS-4C), LV parasternal long axis strain (LVS-L), apical 2 chamber strain (LVS-2C), apical 4 chamber strain rate (LVSR-4C), parasternal long axis strain rate (LVSR-L), apical 2 chamber strain rate (LVSR-2C) were measured automatically by 2D strain software programme (Figure 1). LV global strain (LV-GLS) and LV global strain rate (LV-GLSR) were calculated as mean of

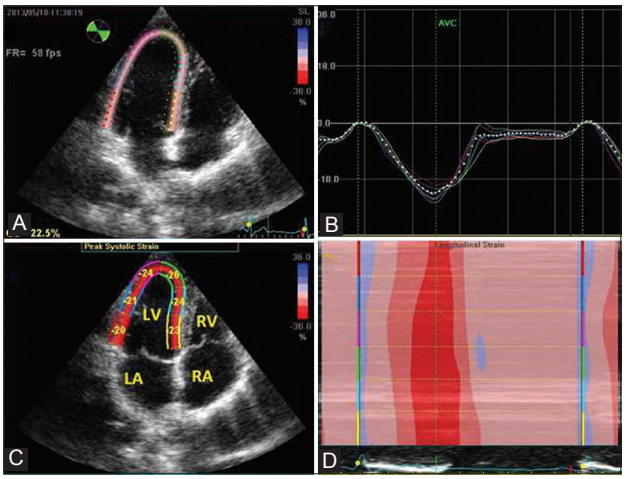

FIGURE 1. Longitudinal strain in an apical four chamber view. A and B show peak systolic strain in colour. C: display average segmental strain in graphs, D: shows peak systolic strain with M-mode

these measurements. Apical and basal short axis rotations were measured by 2D speckle tracking echocardiography, and then LV torsion was calculated as the instantaneous net difference of the basal and apical rotation.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows version 17.0(SPSS, inc, Chicago, IL, USA). Continuous variables are expressed as means ± SD. The Shapiro-Wilk test was used for the normality test of all variables. To compare parametric continuous variables, Independent Student's t test was used; for non-parametric variables the Mann-Whitney U was used. For categorical variables, the Chi Square test was used. Correlations between variables were tested by Pearson or Spearman correlation tests where appropriate. A p-value of < 0.05 was considered to be statistically significant.

RESULTS

The mean disease period of BD patients was 8.8±5.9 years. The demographic, clinical, echocardiographic and laboratory characteristics of the study population were shown in Table 1. There were not any significant differences in terms of age, gender, heart rate, LV diastolic volume, LV systolic volume, LVEF, LA and aorta diameters, while E (p = 0.001), E_m (p = 0.001), A_m (p = 0.004), S (p = 0.003) velocities were differed between the groups.

TABLE 1. Baseline characteristics of patients and controls

Parameters	BD (n=30)	Control (n=25)	p value
Age (years)	28.4±7.0	27.7±4.9	0.714
Female/Male	20/10	16/9	0.823
HR (beat/min)	77.4±7.1	75.0±7.9	0.221
ESR (mm/h)	28.8±9.0	12.0±2.9	<0.001
CRP (mg/L)	1.7±0.4	0.4±0.1	<0.001
IVSTd (mm)	8.8±0.9	8.3±1.1	0.135
LVDV (ml)	73.5±13.6	71.3±13.9	0.772
LVSV (ml)	25.2±4.8	25.3±4.7	0.900
LVEF (%)	65.1±1.1	65.3±1.7	0.450
E (cm/s)	75.6±12.7	94.0±12.8	0.001
A (cm/s)	69.2±9.4	64.3±9.0	0.521
DT (cm/s)	170.9±34.8	193.0±28.6	0.022
S (cm/s)	9.0±0.9	9.9±1.2	0.003
Em (cm/s)	10.5±2.4	14.1±1.8	0.001
Am (cm/s)	9.1±1.4	7.9±1.3	0.004
LA (mm)	31.1±3.3	30.1±2.5	0.461
Ao (mm)	29.1±3.0	29.0±2.3	0.910
Disease duration (years)	8.8±5.9	-	-

$IVST_d$: Interventricular septum diastolic thickness, LVDV: Left ventricular diastolic volume, LVSV: Left ventricular systolic volume, LVEF: Left ventricular ejection fraction, S: Left ventricular peak systolic wave, HR: Heart Rate, peak E: peak mitral velocity of early diastolic filling from transmitrale flow, Peak A indicates peak mitral inflow contraction velocity, E_m: early diastolic filling using DTI. DTI: Doppler tissue imaging, A_m: lately diastolic filling using DTI, DT: Deceleration time, LA: Left atrium, Ao: Aort diameter, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein

Two-dimensional speckle tracking parameters were presented in Table 2. Basal LVR and LVS-L did not differ between the groups. LVS-4C (p = 0.001), LVS-2C (p = 0.001), LV-GLS (p = 0.001), LVSR-4C (p = 0.021), LVSR-L (p = 0.036) and LV-GLSR (p = 0.001) values were found to be lower, while LVR-apical (p = 0.001) and LVTR (p = 0.001) values were significantly higher in patient group than in controls.

In correlation analysis, we found a strong positive correlation between LVR-apical and LVTR (r: 0.84, p < 0.0001). Similarly, LVR-apical and LV-GLS have a good positive correlation (r: 0.44, p < 0.001). There was a significant negative correlation between LVR-apical and E and E_m waves (r: -0.56, r: -0.65, respectively, p < 0.001). There was a weak but statistically significant positive correlation between LVR-apical and LVR-basal values (r: 0.28, p < 0.001). LVR-basal and LV-GLS have weak but statistically significant positive correlation (r: 0.26, p < 0.05). LVTR and LV-GLS also have weak but statistically significant positive correlation. (r: 0.29, p < 0.05) (Figure 2). We found a strong and statistically significant negative correlation between LV-GLS and E and E_m (r: -0.61, r: -0.41, respectively, p < 0.001).

Interobserver and intraobserver agreements were assessed by Bland–Altman analysis. A total of 10 patients were selected randomly to evaluate intra and inter-observer variability. Interobserver variability for strain and strain rate parameters were lower than 5.7% and 6.1%, respectively. Intra-observer variability was approximately lower than 5.7%.

DISCUSSION

In our study, the strain and strain rate were shown to be lower, however, apical rotation and torsion were found to be higher in BD patients than the control group. LV-GLS and LV apical rotation and torsion were positively correlated.

TABLE 2. LV-2D strain, SR, rotation, and torsion measurements of control subject and patients with BD

Parameters	BD (n=30)	Control (n=25)	p value
LVS-4C (%)	18.6±11.5	22.4±2.6	0.001
LVS-L (%)	19.8±2.8	21.1±2.2	0.060
LVS-2C (%)	19.3±1.6	21.0±1.5	0.001
LV-GLS (%)	20.1±1.74	22.2±1.53	0.001
LVSR-4C (s^{-1})	1.20±0.22	1.29±0.21	0.021
LVSR-L (s^{-1})	1.17±0.19	1.26±0.13	0.036
LVSR-2C (s^{-1})	1.25±0.33	1.27±0.13	0.090
LV-GLSR (s^{-1})	1.21±0.22	1.27±0.13	0.001
LVR-apical (degree)	14.1±2.12	10.3±2.17	0.001
LVR-basal (degree)	–5.52±2.81	–0.5,67±1.25	0.450
LVTR (degree)	19.8±1.98	16.1±2.21	0.001

LVS-4C: Left ventricular apical four-chamber strain, LVS-L: Left ventricular parasternal long axis strain, LVS-2C: Left ventricular two-chamber strain, LV-GLS: Left ventricular global strain, LVSR-4C: Left ventricular four-chamber strain rate, LVSR-L: Left ventricular parasternal long axis strain rate, LVSR-2C: Left ventricular two-chamber strain rate, LV-GLSR: Left ventricular global strain rate, LVR-apical: Left ventricular apical rotation, LVR-basal: Left ventricular basal rotation, LVTR: Left ventricular torsion

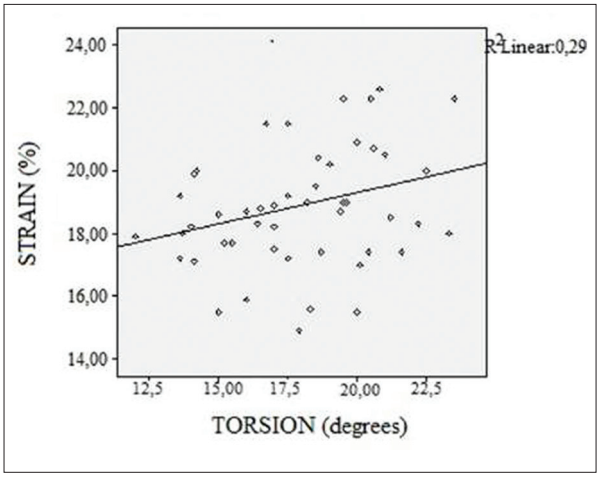

FIGURE 2. Correlations of left ventricular strain with torsion

Clinical cardiac involvement in BD is rarely seen. However, cardiac involvement is commonly asymptomatic and plays an important role in prognosis and increases mortality [12,13]. Vasculitis of the small vessels is the responsible mechanism for cardiac involvement in BD [14]. Accumulation of focal fibrinoid material and fibroelastic proliferation were detected in small arteries and arterioles of these patients [15]. Vasculitic events in small arteries and arterioles of coronary circulation can cause coronary thrombus and aneurysm formation leading myocardial ischemia and fibrosis which can affect systolic and diastolic functions of the myocardium [16,17]. LV diastolic function is impaired firstly due to vasculitic lesions in BD. In two studies performed by radionuclide ventriculography, LV peak filling velocity was found to be lower than normal in 50% and 37.5% of the patients, respectively, indicating diastolic dysfunction in these patients [18,19]. As a result, it is crucial to detect subclinical LV dysfunction in BD patients. Nevertheless, radionuclide ventriculography is not a practical and easily available test. Most of the previous studies have evaluated the LV diastolic parameters in BD. In our study, we aimed to determine the myocardial changes in BD by 2D strain which was shown to be superior to TDI and Doppler strain in previous studies.

TDI is characterized with the limitations of angle dependence, limited spatial resolution, and deformation analysis in one dimension [20]. Two dimensional STE is a good method which has been developed recently, can evaluate myocardial functions regionally and globally independently from angle and may be used for detecting different cardiac pathologies. This new technique enables to better evaluate myocardial contraction and relaxation [21-24]. In our study, LVS-4C, LVS-2C, LV-GLS measured by STE were significantly lower in the patients than the control group in addition to the diastolic dysfunction findings detected by conventional Doppler echocardiography and TDI. Additionally, LV-GLSR, LVSR-4C, LVSR-L were found to be significantly lower in the patients than the control group. These findings support the simultaneous presence of both systolic and diastolic dysfunction in BD. Supporting our results, Yagmur et al. [25] previously found that regional and mean longitudinal strain were lower in their patient group than the controls.

Another finding of our study was that LVR-apical and LVTR were higher in BD patients than the control group. The base of the heart makes clockwise rotation however the apex makes counterclockwise rotation [26,27]. The rotation procedes from apex to the base. LV torsion is calculated as the instantaneous net difference of the basal and apical rotation. LV torsion is related to myofibrils. Since it is related to myofibrils, it contributes to LV filling [28,29]. Thus, LV torsion, as LV myocardial deformation, has great importance in determination of dysfunction. LV rotation and torsion increase in impaired relaxation and decrease in restrictive pattern and pseudonormalization [30]. In our study, we found that LV torsion and apical rotation were higher in BD and this result is related to LV diastolic dysfunction (grade 1: impaired relaxation). Depending on this result, we can conclude that LV rotation grade and torsion can determine diastolic dysfunction in early stages of BD. Additionally, LV-GLS and LV-GLSR values were decreased in BD. This finding is important in determination of subclinical LV dysfunction. In our study, even if it was weak, a correlation was detected between LV-GLS and LVTR. In conclusion, we can use all of these parameters in determination of subclinical LV dysfunction.

The major limitations of our study are relatively small number of the sample size and the inequality of thenumbers of individuals between the patient and the control groups and the variability of the treatment between patients. Another limitation is; only longitudinal strain and strain rate parameters were measured in assessment of LV functions however radial and circumferential strain and strain rate were not used. Since the effect of subclinical dysfunction on prognosis was not among our study objectives, any follow up was not planned. So, the effect of subclinical dysfunction on the prognosis remains unclear. Apart from the echocardiography, although some parameters such as NT-proBNP [25] were studied, no laboratory test could reliably predict the subclinical LV dysfunction in patients with BD is the other limitation of our study.

CONCLUSION

Although cardiac involvement is rare, it has strong prognostic importance in BD. In our study, LV-GLS and LV-GLSR values were significantly lower, however, LVTR and LVR-apical values were found to be higher in patients with BD. These results are related to subclinical LV dysfunction. Nevertheless, additional studies are needed for practical applications in clinic.

DECLARATION OF INTEREST

The authors declare that there is no conflict of interest.

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