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EVALUATION OF DIASTOLIC FUNCTIONS IN PATIENTS WITH BEHCET'S DISEASE: A TISSUE DOPPLER STUDY

Behçet Hastalarında Diyastolik Fonksiyonların Değerlendirilmesi: Bir Doku Doppler Çalışması

ABSTRACT

Objectives: The aim of this study was to evaluate diastolic functions and myocardial performance index (MPI) in patients with Behcet's disease (BD).

Methods: Thirty-one BD patients (mean age 34.4±10.5 years) and 31 control subjects (mean age 33.2±10.3 years) were enrolled in this study. Left ventricular and right ventricular diastolic functions were assessed by conventional Doppler and tissue Doppler (TDI) methods, and MPI was also calculated. The relationship between these parameters and disease duration was evaluated.

Results: In conventional Doppler echocardiography, Mitral A-wave velocity and deceleration time were higher, and E/A ratio was lower in patients with BD (p=0.002, p=0.02, and p=0.006, respectively). Mitral E-wave velocity and isovolumetric relaxation time were comparable between groups (p>0.05). In TDI examination, E′/A′ ratio measured from lateral mitral annulus was lower, and A′ velocity measured from lateral tricuspid annulus was higher in patients with BD (p=0.03 and p=0.02, respectively). Other mitral annular TDI (E′, A′, S′, E/E′ ratio, and MPI) and tricuspid lateral annular parameters (S′, E′, E′/A′ ratio and MPI) were similar between two groups (p>0.05). In correlation analysis, lateral mitral annulus E′/A′ ratio were inversely correlated with disease duration in patients with BD (r = -0.54, p=0.002).

Conclusion: Left and right ventricular diastolic function parameters were significantly different in patients with BD and controls. Diastolic function parameters were significantly associated with disease duration and echocardiographic follow-up may be useful in these patients.

Key words: Behcet's disease, tissue Doppler echocardiography, myocardial performance index

ÖZET

Amaç: Bu çalışmada, Behçet hastalarında diyastolik fonksiyon parametreleri ve miyokard performans indexi (MPİ) değerlendirildi.

Yöntem: Otuz bir Behçet hastası (ort. yaş 34.4±10.5 yıl) ve 31 kontrol vakası (ort. yaş 33.2±10.3 yıl) çalışmaya alındı. Sol ventrikül ve sağ ventrikül diyastolik fonksiyonları konvansiyonel Doppler ve doku Doppler görüntüleme (DDG) yöntemiyle değerlendirildi. DDG yöntemiyle MPİ hesaplandı. Bu parametreler ile hastalık süresi arasındaki ilişki incelendi.

Bulgular: Behçet hastalarında konvansiyonel Doppler ekokardiyografi ile mitral A dalga hızı ve deselerasyon zamanı yüksek, E/A oranı düşük idi (sırasıyla, p=0.002, p=0.02, ve p=0.006). Gruplar arasında mitral E dalga hızı ve izovolümetrik gevşeme zamanı benzerdi (p>0.05). Behçet hastalarında, DDG yöntemiyle lateral mitral anülüsten ölçülen E′/A′ oranı düşük, lateral triküspit anülüsten ölçülen A′ hızı yüksek idi (sırasıyla, p=0.03 and p=0.02). Diğer mitral anüler DDG parametreleri (E′, A′, S′, E/E′ oranı, ve MPİ) ve lateral triküspit anüler parametreleri (S′, E′, E′/A′ oranı ve MPİ) gruplar arasında benzerdi (p>0.05). Korelasyon analizinde, Behçet hastalarında lateral mitral annulus E′/A′ oranı hastalık süresiyle zıt olarak korele idi (r=-0.54, p=0.002).

Sonuç: Behçet hastalarında kontrol grubuna göre sol ve sağ ventrikül diyastolik fonksiyonları anlamlı olarak farklıdır. Bu hasta grubunda diyastolik fonksiyon parametreleri hastalık süresiyle ilişkili olup ekokardiyografik takip faydalı olabilir.

Anahtar Kelimeler: Behçet hastalığı, doku Doppler görüntüleme, miyakard performans indeksi

INTRODUCTION

Behcet's disease (BD) is a systemic inflammatory disease of unknown etiology characterized by recurrent oral and genital ulcers, uveitis and systemic involvement (1). Cardiovascular manifestations including endocarditis, myocarditis, pericarditis, acute myocardial infarction,

aortic aneurysm, intracardiac thrombosis, congestive cardiomyopathy, valvular dysfunction and diastolic dysfunction have been reported (2). These cardiac manifestations are quite rare and mostly based on case-control studies (2). It is well known that inflammation markers are increased in patients with BD (3). Also, increased inflammatory process is significantly associated with myocardial fibrotic changes (4,5). These alterations may lead to significant diastolic dysfunction without systolic dysfunction in patient with BD. However, there are conflicting findings about the presence of diastolic dysfunction in these patients (3,6-12).

Tissue Doppler imaging (TDI) is a new Doppler method that can provide measurements of regional systolic and diastolic myocardial velocities with a high temporal and spatial resolution, and it is particularly useful in the identification of abnormalities of diastolic function (13). This technique has been shown to be relatively independent of the confounding effects of conventional Doppler echocardiography from the several factors such as pseudonormalization, rate of myocardial relaxation, and volume status (14). Additionally, myocardial performance index (MPI) calculated with TDI is a helpful parameter to evaluate systolic and diastolic ventricular function (15).

In the present study, we investigated whether TDI and MPI could provide more information than conventional echocardiography about left and right ventricular function in patients with BD.

MATERIALS AND METHODS

Patients

Thirty-one patients with BD (10 females, 21 males; mean age 34.4±10.5 years) according to the International Study Group criteria for BD (16) were included from the rheumatology out-patient clinic. Also, 31 age and gender-matched healthy subjects (11 females, 20 males; mean age 33.2±10.3 years) were included as control. Physical examination, medical history of patients and blood biochemistry were evaluated in all groups to exclude systemic diseases. The clinical manifestations and medications of the BD patients are summarized in Table 1. None of the patients had any of the active disease manifestations during echocardiographic evaluation state (no symptoms for at least 1 month).

Patients and controls with a history of coronary artery disease, arterial hypertension, diabetes mellitus, left ventricular (LV) ejection fraction (EF) less than 50%, primary cardiomyopathy, valvular heart disease, and bundle branch block, atrioventricular conduction abnormalities on electrocardiogram, thyroid dysfunction, anemia, hypercholesterolemia, renal failure, pulmonary disease and poorly quality echocardiographic imaging were excluded from the study. All of the patients were in sinus rhythm and none of them were taking cardiac medicines. Fasting blood glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride levels, duration of disease and CRP level (mg/dl) were noted from medical record. Written informed consent was obtained from each subject. The institutional ethics committee approved the study protocol.

Echocardiographic examination

Echocardiographic evaluation was performed by using a Vivid 7 Doppler echocardiographic unit with a 2,5 MHz phased array transducer (GE, Horten, Norway). The LV diameter, wall thickness, LV EF, aortic root, left atrium and pulsed-wave Doppler parameters were measured according to the American Society of Echocardiography's recommendations (17). LV mass was calculated with Devereux formula (18) and was indexed to body surface area.

Mitral flow velocity was obtained from the apical four-chamber view with the pulsedwave technique by placing the sample volume between the tips of the mitral leaflets for conventional diastolic parameters of the left ventricle. The following parameters were calculated: maximal velocity of early diastolic filling (E), maximal velocity of atrial diastolic filling (A), E/A ratio and deceleration time of early diastolic filling (DT). Left ventricle isovolumetric relaxation time (IVRT) was also obtained from the apical five-chamber view through the continuous- wave technique by placing the sample volume between mitral and aortic leaflets. Tissue Doppler imaging (TDI) was performed with transducer frequencies of 1.8– 3.6 MHz with minimum optimal gain as possible to obtain the best signal to noise ratio. In the apical four chamber view, a 5 mm pulsed Doppler sample volume was placed at the level of the lateral mitral annulus and lateral tricuspid annulus. Mitral annular peak systolic (S′), early diastolic (E′), late diastolic (A′) velocities and late to early velocity ratio (E′/A′) were measured at the lateral corner of the mitral and tricuspid annulus (19). E/E′ ratio was also calculated to provide an estimation of LV filling pressures (20). The left and right ventricular MPI was calculated as isovolumetric relaxation time plus isovolumetric contraction time divided by the ejection time with TDI method (15). All echocardiographic examinations were performed by an experienced cardiologist by the average of three measurements, and images were recorded digitally recorded.

Intraobserver variability was assessed in 10 selected subjects at random from the patient study group by repeating the measurements under the same basal conditions. To test the interobserver variability, recorded images were analyzed by a second observer who was unaware of the results of the first examination. The values of coefficient of variation intra and interobserver of echocardiographic measurements ranged from 3% to 9%.

Statistical Analysis

All analyses were conducted using SPSS 9.0 (SPSS for Windows 9.0, Chicago, IL). All continuous variables were expressed as mean ± standard deviation; categoric variables were defined as percentages. Categoric data were compared with the chi-square test. Mean values of continuous variables were compared between groups using the Student t test or Mann–Whitney U test, according to whether normally distributed or not, as tested by the Kolmogorov–Smirnov test. Pearson's correlation coefficients were used to assess the strength of the relationship between continuous variables. $p < 0.05$ was considered significant.

RESULTS

Clinical characteristics and echocardiographic findings of the subjects are shown in Table 1. Age, sex, BSA, smoking status, systolic and diastolic blood pressure, heart rate, LV end diastolic

Table 1: The demographic and clinical characteristics of the patients and control subjects.

	Patients (n=31)	Controls (n=31)	p
Age (years)	34.4±10.5	33.2±10.3	NS
Female/male (n/n)	10/21	12/20	NS
BSA (m^2)	1.7±0.4	1.8±0.2	NS
Smokers (n)	5	5	NS
SBP (mmHg)	110.23±15.2	108.6±9.3	NS
DBP (mmHg)	71.0±7.9	71.3±6.5	NS
Heart rate (beats/min)	76.6±11.4	72.7±9.4	NS
CRP (mg/L)	7.7±7.3	3.3±0.1	0.01
Disease duration (years)	6.6±7.5	-	
LV diastolic diameter (mm)	46.2±8.3	47.6±4.5	NS
LV systolic diameter (mm)	29.8±3.6	30.0±4.1	NS
IVS thickness (mm)	9.7±1.6	9.4±1.3	NS
PW thickness (mm)	8.8±1.4	8.3±1.3	NS
LV mass index (g/m^2)	87.8 ± 16.1	85.6 ± 17.2	NS
Left atrial dimension (mm)	34.1±4.7	31.7±5.0	NS
LV EF (%)	67.5±5.9	67.6±5.7	NS

BSA: body surface area; SBP: systolic blood pressure; DBP: diastolic blood pressure; CRP: C-reactive protein; LV: left ventricular; IVS: interventricular septum; PW: posterior wall thickness; EF: ejection fraction.

Table 2: Comparison of conventional and tissue Doppler echocardiographic measurements.

	Patients (n=31)	Controls (n=31)	p
Conventional Doppler Measurements			
Mitral E velocity (cm/s)	79.5±16.9	81.1±18.0	NS
Mitral A velocity (cm/s)	64.1±14.5	59.6±8.4	0.002
E/A	1.28±0.29	1.50±0.31	0.006
E/A<1 (%)	16	3	0.09
DT (ms)	204.6±28.3	190.7±14.5	0.02
IVRT (ms)	89.3±12.2	88.0±11.5	NS
Tissue Doppler Measurements			
LV lateral annulus			
S′ (cm/s)	10.9±2.9	11.5±1.8	NS
E′ (cm/s)	14.1±3.9	16.1±4.4	NS
A′ (cm/s)	10.7±3.0	9.5±2.3	NS
E′/A′	1.44±0.63	1.79±0.64	0.03
E′/A′<1 (%)	26	10	0.08
E/E′	5.96±1.57	5.26±1.28	NS
MPI (%)	48.8±7.7	49.5±7.0	NS
RV tricuspid annulus			
S′ (cm/s)	14.6±2.7	14.0±2.1	NS
E′ (cm/s)	13.4±2.7	14.6±3.4	NS
A′ (cm/s)	15.2±3.8	13.0±3.4	0.02
E′/A′	0.92±0.25	1.18±0.33	NS
E′/A′<1 (%)	30	23	NS
MPI (%)	46.8±5.5	44.6±6.4	NS

LV: Left ventricular; DT: Mitral E-wave deceleration time; IVRT: isovolumetric relaxation time; S′: myocardial systolic velocity; E′: myocardial early diastolic velocity; A′: myocardial late diastolic velocity; MPI: myocardial performance index; NS: not significant.

dimension, LV end-systolic dimension, LV mass index, left atrium dimension and LV EF were similar between the two groups ($p > 0.05$). Plasma level of CRP was significantly higher in the patients with BD. The mean disease duration was 6.6±7.5 years.

The results of conventional and tissue Doppler measurements and are summarized in Table 2. Deceleration time, mitral A velocity and E/A ratio were significantly different between the groups (all $p<0.05$). Other conventional Doppler measurements were comparable between the groups ($p>0.05$).

The E′ velocity and A′ velocity obtained from lateral mitral annulus were tended to be different between the groups ($p>0.05$). Only E′/A′ ratio was significantly lower in patients with BD ($p=0.03$). Other TDI parameters including mitral E/E′ ratio, S′ and MPI values were similar between patients and control subjects ($p>0.05$). Also, only A′ velocity obtained from lateral trisuspid annulus were significantly higher patients group ($p=0.02$). Other TDI parameters (S′, E′, E′/A′ ratio and MPI) obtained from lateral tricuspid annulus were similar between patients and control subjects.

In correlation analysis, the mitral E′/A′ ratio obtained from lateral mitral annulus were inversely correlated with duration of disease ($r=-0.54$, $p=0.002$) in patients with BD (Figure 1).

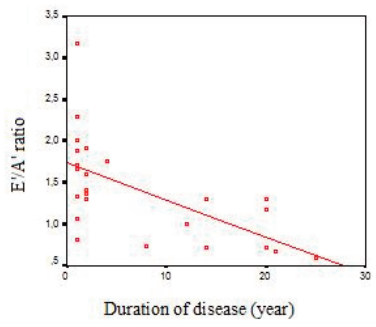

Figure 1: The figure shows a negative correlation between the early/late diastolic mitral annular velocitiy ratio (E′/A′) with duration of Behcet's disease ($r = -0.54$, $p = 0.002$).

DISCUSSION

This study demonstrated that there were early diastolic alterations between BD patients and controls. Left ventricular diastolic function parameters were associated with disease duration. Tissue Doppler imaging derived MPI was comparable in the patients and controls.

Increased inflammatory activity and disturbance of coronary microcirculation may lead to myocardial fibrosis in patients with BD (3-5,11). Several clinical studies have shown that there is a close relation between increased inflammatory activity and diastolic dysfunction parameters (3,11). Therefore, impairment of diastolic functions might have occurred in patients with BD. However, rather controversial data have been reported in several studies investigating the effect of BD on diastolic function (3,6-12). Tunc et al. and Tavil et al. have found no significant diastolic function abnormality in patients BD (6,12). Likewise, it has been reported that LV diastolic functions were similar both rest and at the end of exercise in these patients (8). However, opposite findings suggesting significant diastolic function abnormality with conventional and/or TDI methods reported in these patient population (3,7,9-11). Additionally, an inverse association between serum inflammation levels and mitral annular E′/A′ ratio was displayed in previous studies (3,11). We could not such a relation, this may result from using different inflammatory marker (CRP, high sensitive CRP, homocysteine and cellular adhesion molecules).

Recently, Tavil et al. (12) have demonstrated that only TDI derived MPI was increased other diastolic function parameters were similar in patients with BD. Oppositely, we revealed that diastolic function parameters of left and right ventricles were significantly different in patients with BD, and TDI derived MPI was comparable between patients and controls. Also, mitral annular E′/A′ ratio was positively related with disease duration in our study. The probable reasons for the difference between our results and published research on diastolic dysfunction may be result from differences in BD patient populations (mean age, disease duration, using drugs affecting cardiac function, the activity of disease and concomitant disease, etc.), numbers of patients and echocardiographic methods.

The E/E′ ratio was found to correlate significantly with LV end-diastolic pressure and diastolic dysfunction (20). If the E/E′ ratio below 8 or above 15, it can confidently separate normal from elevated filling pressures. The most important limitation of this index is seen in patients with a value between 8 and 15. In the present study, we do not have any value higher than 15.

The major limitation of our study was small population size due to single centre and tight inclusion criteria. Therefore, larger patient populations are needed to confirm our finding.

In conclusion, detection of abnormalities in ventricular diastolic function might provide a means of identifying patients at risk for progressive heart failure. The early detection of ventricular dysfunction may be important in clinical practice when assessing the prognosis and optimizing treatment. In our study revealed that there were significantly early diastolic alterations in both ventricles between BD patients and controls. Also, mitral annular E′/A′ ratio was significantly associated with duration of disease.

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