



Tissue Doppler, Strain, and Strain Rate Echocardiography in the Evaluation of Left Ventricular Functions in Patients with Asymptomatic Ankylosing Spondylitis

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ABSTRACT

Introduction: Ankylosing spondylitis (AS) is a chronic inflammatory disease with extraarticular involvement. Approximately 2%-10% of AS patients have cardiac involvement. These patients have an increased risk of cardiovascular mortality compared to normal individuals. This study aimed to evaluate subclinical cardiac involvement in AS patients using the current strain (S) and strain rate (SR) echocardiography (echo) techniques.

Patients and Methods: Our study was conducted between January 2017 and February 2018 involving 29 asymptomatic patients with AS and 26 healthy controls. Systolic and diastolic functions, tissue Doppler measurements, and left ventricular S and SR values were obtained by 2D echo and compared between groups.

Results: Demographic variability was similar between AS and control groups. Echo results showed statistically higher right ventricular end-diastolic and left atrial diameter in the AS group. Mean basal anterolateral, midanterolateral, basal inferoseptum, basal anterior, and left ventricular S values were significantly lower in the AS group. Mean anterolateral, basal inferoseptum, basal inferior, and mean left ventricular SR values were significantly lower in the AS group.

Conclusion: We found that left ventricular functions were impaired at the subclinical level by strain imaging technique in AS patients. We believe that the investigation of subclinical myocardial dysfunction in AS by more sensitive and novel methods such as strain imaging technique will be useful in determining myocardial functions of patients.

Key Words: Ankylosing spondylitis; left ventricular functions; strain; strain rate; subclinical myocardial damage

Asemptomatik Ankilozan Spondilitli Olgularda Sol Ventrikül Fonksiyonlarının Değerlendirilmesinde Doku Doppler, Strain ve Strain Rate Ekokardiyografi

ÖZET

Giriş: Ankilozan spondilit (AS) eklem dışı tutulum yapabilen kronik enflamatuvar bir hastalıktır. AS hastalarının yaklaşık %2-10'unda kardiyak tutulum mevcuttur. Bu hastaların normal bireylere göre kardiyovasküler mortalite riski artmıştır. Bu çalışmada AS hastalarında subklinik kardiyak etkilenmeyi, güncel bir kardiyak görüntüleme yöntemi olan Strain (S) ve Strain Rate (SR) ekokardiyografi (EKO) tekniklerini kullanarak değerlendirmek amaçlanmıştır.

Hastalar ve Yöntem: Çalışma, Ocak 2017-Şubat 2018 tarihleri arasında, AS tanısı alan 29 asemptomatik hasta ve 26 sağlıklı bireyi içeren kontrol grupları ile yapıldı. Bireylerin sistolik ve diyastolik fonksiyonları, doku Doppler ölçümleri, sol ventrikül strain ve strain rate değerleri 2D EKO ile elde edildi ve gruplar arasında karşılaştırıldı.

Bulgular: Hasta ve kontrol grubunun demografik değişkenlikleri benzerdi. EKO sonuçları karşılaştırıldığında sağ ventrikül diyastol sonu çapı ile sol atriyum çapı, hasta grubunda istatistiksel olarak anlamlı büyüklüğe sahipti. Strain değerleri karşılaştırıldığında, bazal antero-lateral, mid antero-lateral, bazal infero-septum, bazal anteriyör ve sol ventrikül ortalama S değerleri, hasta grubunda anlamlı derecede daha düşüktü. Strain Rate değerleri karşılaştırıldığında ise, mid antero-lateral, bazal infero-septum, bazal inferiyör ve ortalama sol ventrikül SR değerleri, hasta grubunda daha düşüktü.

Sonuç: Çalışmada, AS hastalarında strain görüntüleme tekniği ile sol ventrikül fonksiyonlarının, subklinik düzeyde bozulduğu saptanmıştır. AS'daki subklinik miyokardiyal fonksiyon bozukluğunun, strain görüntüleme tekniği gibi daha hassas ve yeni yöntemlerle araştırılmasının hastaların miyokardiyal fonksiyonlarını belirlemede faydalı olacağını düşünüyoruz.

Anahtar Kelimeler: Ankilozan spondilit; sol ventrikül fonksiyonları; strain; strain rate; subklinik miyokardiyal hasar

Cite this article as: Tahta M, Yalim Z, Avcı A. Tissue doppler, strain, and strain rate echocardiography in the evaluation of left ventricular functions in patients with asymptomatic ankylosing spondylitis. Koşuyolu Heart J 2020;23(1):15-21.

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Submitted: 10.09.2019

Accepted: 14.12.2019

Available Online Date: 30.04.2020

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INTRODUCTION

Ankylosing spondylitis (AS) is an inflammatory autoimmune disease of unknown etiology associated with human leukocyte antigen (HLA)-B27, which belongs to the group of spondyloarthropathies (SpA)⁽¹⁾. This group of diseases includes more than one disease with different but related and heterogeneous signs and symptoms⁽²⁾. AS may include the heart, gastrointestinal tract, lungs, and neurological and genitourinary system.

Cardiac involvement in AS is around 2%-10% and it is known to most frequently cause aortic regurgitation⁽³⁾. This is followed by conduction abnormalities, mitral valve involvement, and myocardial and pericardial involvement⁽⁴⁾. Myocardial changes in AS have been studied in several studies, and a significantly increased frequency of systolic and diastolic dysfunction in these patients has been reported in some published cases⁽⁵⁻⁷⁾. However, there is still insufficient evidence on how cardiac functions of asymptomatic individuals are affected.

Classical echocardiographic evaluation methods provide highly subjective information in determining ventricular functions. Strain (S) and strain rate (SR) echocardiographic method has become increasingly important in recent years. It can provide more objective data in the global and segmental evaluation of left and ventricular systolic functions⁽⁸⁾. It is known that classical echocardiographic evaluation is insufficient in determining cardiac involvement which is very common in patients with AS. This study aimed to investigate the subclinical myocardial activity in AS by deformation and SR echocardiography (echo) method.

PATIENTS and METHODS

Ethics committee approval was received for this study from the Clinical Research Ethics Committee of the Afyonkarahisar Health Sciences University (Decision Number: 2019/222; Decision Date: June 17, 2019).

Our study was carried out between January 2017 and February 2018 at Afyonkarahisar Health Sciences University Faculty of Medicine Cardiology Clinic. Thirty patients diagnosed with AS using the modified New York criteria and 26 healthy individuals were included. Detailed information about the purpose and method of the study were provided, and verbal and written consent obtained for participation. One out of 30 patients whose consent was obtained was excluded based on exclusion criteria.

We excluded patients with history of congenital, rheumatic, valvular, coronary, myocardial, and pericardial diseases, with rhythm and conduction disorders, and using drugs that affect the cardiovascular system functions or may change the measurement results. Patients over the age of 60 and under 18 years old or with hypertension, type 1 and 2 diabetes mellitus, malignancy, and chronic or systemic diseases were also excluded.

Echo and Doppler examinations were performed with a Philips HD 11 XE (Germany, 2008) echo device using a 3.5 MHz transducer. All echo examinations were conducted by the same operator. After the patients were monitored electrocardiographically, the images were obtained using appropriate gain settings and parasternal long axis, short axis, and apical 2, 3, and 4 cavity approaches. M-mode, 2D, pulsed-wave Doppler, and color Doppler techniques were used to evaluate cardiac measurements and movements. Measurements were made in line with the recommendations of the American Echocardiography Association⁽⁹⁾.

Aortic insufficiency severity was graded by the proportion of the diameter of the current fleeing in the parasternal long axis to the annulus diameter at the level of the aortic valve⁽¹⁰⁾, while mitral insufficiency severity was graded by the proportion of leakage current area to the atrium area⁽¹¹⁾. For the evaluation of diastolic functions, pulsed-wave Doppler sign (sample volume) was placed on the mitral valve in the apical image, and E wave velocity, E wave deceleration times (DTs), and E/A ratios were measured from the region where the velocities could be most clearly monitored. Isovolumetric relaxation time (IVRT) was measured by the time interval between the end of aortic flow and the onset of mitral flow.

Tissue Doppler imaging (TDI) was obtained from sections where the mitral annulus meets the septum and lateral walls through 4 apical spaces. Causes of segmental wall motion disorder in AS and control groups were eliminated as much as possible and TDI measurements were limited to 2 points. For left ventricular longitudinal S and SR measurements, a motion image of 160-210 fps each of the apical 2, 3, and 4 cavity images that contain at least 4 cardiac cycles in tissue velocity imaging mode at the end of expiratory breath was recorded⁽¹²⁾. The records were studied with Strain Quantification (Phillips Co., USA) software. Due to high measurement errors, measurements were not taken from apical sections and data was collected from 8 segments, and peak systolic S and SR measurements were performed in each segment (Figure 1).

SPSS (Statistical Package for the Social Sciences) software version 15.0 (SPSS Inc., Chicago, IL) was used for statistical evaluation. The suitability of variables to normal distribution was evaluated by visual and analytical methods. Descriptive analyses were performed using mean and standard deviation for normally distributed variables and median values for non-normally distributed variables. Mann-Whitney U test was used to evaluate the difference between the groups, as the number of cases in the study groups was below 30. $p < 0.05$ was considered statistically significant.

RESULTS

This study included 29 AS patients (23 men and 6 women) and 26 controls (20 men and 6 women). Clinical features such

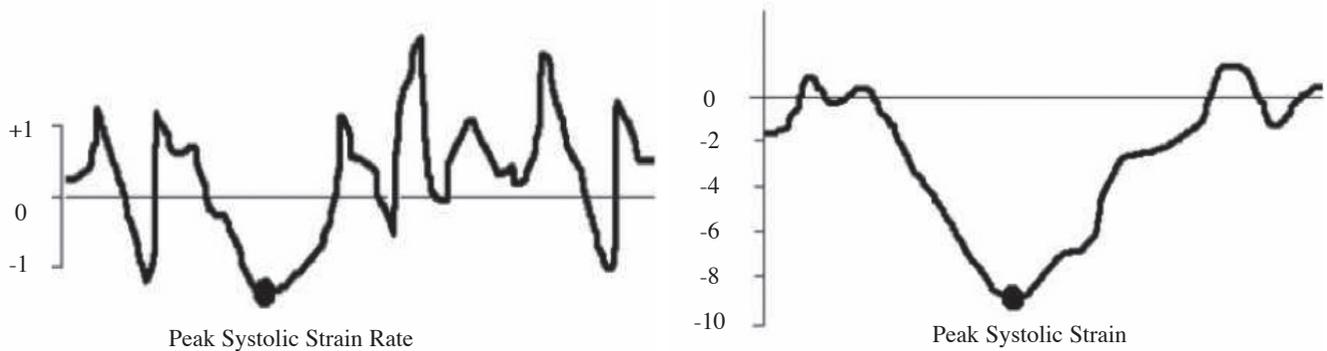


Figure 1. Peak systolic S and SR values⁽¹³⁾.

as age, gender, body mass index, general age, and systolic and diastolic blood pressures were statistically significant among groups. Demographic variables and electrocardiographic findings of AS and control groups are presented in Table 1.

No statistically significant differences were observed in the measurements obtained by M-mode and 2D echo (diastole and end-systolic diameters, septum and posterior wall thickness, LVEFs, and aortic diameters) between AS and control groups. The right ventricular diastole diameter ($p= 0.009$) and left atrium diameter ($p= 0.046$) were significantly higher in the AS

group. Aortic valve involvement was observed in a total of 5 patients (17.24%), including 1 degree AY and aortic dilatation in 4 patients and aortic valve thickening in 4 patients. Aortic valve involvement was not observed in the control group. Statistically significant difference was found between the groups ($p= 0.039$). Aortic valve involvement and echocardiographic measurements of AS and control groups are given in Table 2.

There was no statistically significant difference in mean E and A wave velocities, E/A ratios, and DT obtained to evaluate diastolic functions of the groups. IVRT value of diastolic varia-

Table 1. Demographic characteristics of ankylosing spondylitis and control groups

Variables	AS (n= 30)	Control (n= 30)	p
Gender (M/W), n (%)	23/6 (79.32/20.68)	20/6 (76.92/3.08)	0.832
Age (year)	39.86 ± 9.38	39.00 ± 11.96	0.432
BMI (kg/m ²)	23.35 ± 3.28	23.79 ± 1.78	0.973
Systolic blood pressure (mmHg)	114.16 ± 5.05	108.50 ± 8.37	0.107
Diastolic blood pressure (mmHg)	69.17 ± 10.70	66.19 ± 6.29	0.293
Heart rate (beats/min)	74.75 ± 10.62	67.69 ± 7.58	0.004*
PR interval (sn)	0.16 ± 0.01	0.15 ± 0.01	0.234
QRS (sn)	0.10 ± 0.02	0.10 ± 0.01	0.412
Complete right branch block	1	0	0.113
Incomplete right branch block	2	0	0.097
Fasting glucose (mg/dL)	87.57 ± 10.61	90.86 ± 7.63	0.244
Creatinine (mg/dL)	0.73 ± 0.12	0.75 ± 0.20	0.160
Total cholesterol (mg/dL)	177.24 ± 9.05	183.04 ± 9.66	0.330
HDL cholesterol (mg/dL)	39.54 ± 6.76	42.32 ± 6.92	0.105
LDL cholesterol (mg/dL)	100.92 ± 23.45	104.41 ± 8.88	0.463
Triglyceride (mg/dL)	119.75 ± 35.35	127.69 ± 31.41	0.063
Sedimentation	21.89 ± 17.57	17.57 ± 4.52	< 0.01*
CRP (mg/dL)	1.82 ± 2.35	0.63 ± 0.23	0.04*

* $p < 0.05$, statistical significance. BMI: Body mass index, CRP: C-reactive protein, M: Man, W: Woman.

Table 2. Echocardiographic findings of ankylosing spondylitis (AS) and control groups

Variables	AS (n= 30)	Control (n= 30)	p
LVEDD (mm)	49.10 ± 4.61	48.14 ± 4.43	0.401
LVESD (mm)	30.64 ± 3.29	30.28 ± 3.28	0.428
LVEF Simpson (%)	66.99 ± 5.18	64.56 ± 12.42	0.692
IVS (mm)	10.52 ± 1.23	9.71 ± 1.39	0.310
PW (mm)	10.10 ± 1.02	9.40 ± 2.03	0.273
LA volume (mL/m ²)	37.86 ± 3.65	33.13 ± 2.60	0.046*
Aortic Root (mm)	29.14 ± 3.78	27.60 ± 27.60	0.127
Aortic Valve Involvement	5 (17.24%)	0	0.039*
Mitral E (m/s)	81.71 ± 17.01	77.64 ± 16.57	0.516
Mitral A (m/s)	68.51 ± 15.10	63.66 ± 13.69	0.121
Mitral E/A	1.19 ± 0.34	1.21 ± 0.29	0.126
Deceleration time (msn)	193.17 ± 31.72	205.23 ± 23.43	0.110
Isovolumetric Rest Time (msn)	96.24 ± 11.99	82.31 ± 10.98	< 0.001*
Mitral E/Em	8.81 ± 2.27	7.96 ± 2.07	0.054*
LATSm (cm/s)	9.31 ± 1.95	9.17 ± 1.57	0.380
LATEm (cm/s)	13.23 ± 2.76	14.58 ± 2.89	0.057
LATAm (cm/s)	11.40 ± 2.53	9.89 ± 2.39	0.060
SEPSm (cm/s)	9.01 ± 1.06	7.87 ± 1.46	0.125
SEPEm (cm/s)	9.33 ± 2.37	11.57 ± 2.70	0.128
SEPA m (cm/s)	9.21 ± 1.44	9.96 ± 1.26	0.095
Diastolic dysfunction	7 (24.13%)	0	0.02*

* p< 0.05, statistical significance. LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end systolic diameter, LVEF: Left ventricular ejection fraction, IVS: Interventricular septum, PW: Posterior wall, LA: Left atrium, E: Early diastolic mitral flow velocities, A: Late diastolic mitral flow velocities, Em: Tissue Doppler early diastolic mitral annular velocities, LATSm: Lateral systolic mitral annular velocities, LATEm: Lateral early diastolic mitral annular velocities, LATAm: Lateral late diastolic mitral annular velocities, SEPSm: Septal systolic mitral annular velocities, SEPEm: Septal early diastolic mitral annular velocities, SEPA m: Septal late diastolic mitral annular velocities, LV: Left ventricle, LAT: Lateral, SEP: Septal.

bles was significantly higher in AS than in control group (96.24 ± 11.99 ms and 82.31 ± 10.98 ms, respectively) (p< 0.001). No statistically significant difference was found between S, E, and A wave velocities taken from the septal and lateral annulus. There were 7 patients with diastolic dysfunction in the AS group (24.13%) while no diastolic dysfunction was observed in the control group. Increased diastolic dysfunction rate was statistically significant in AS group (p= 0.02). Diastolic functions and tissue Doppler measurements are presented in Table 2.

S and SR data of the left ventricle were obtained from a total of 8 segments. Apical segments were excluded due to angle incompatibility. Basal anterolateral, midanterolateral, basal inferoseptum, and basal anterior S values were significantly lower in AS group than control group. Mean left ventricular S rate, which can be considered as an indicator of global left ventricular systolic function, was also significantly lower in the AS

group. Midanterolateral, basal inferoseptum, basal inferior, and mean left ventricular SR values were found to be statistically significant in the AS group (Table 3).

DISCUSSION

Patients with AS have 1.6-1.9-fold increased mortality compared to the normal population. Cardiac mortality in patients with AS is estimated to be around 20%-40%^(14,15). Although the cause of increased cardiovascular mortality in these patients is not clearly known, chronic inflammatory process and autoimmunity have been shown to play a role⁽¹⁶⁾. In our study, we found that both systolic and diastolic functions are impaired in asymptomatic AS patients. We believe that although not used in routine practical evaluation, S and SR measurements will contribute to showing myocardial damage especially in the AS group and if necessary, early treatment of patients may be beneficial for increased cardiovascular mortality.

Table 3. Strain and strain rate echocardiographic findings of ankylosing spondylitis (AS) and control groups

Variables	AS (n= 30)	Control (n= 30)	p
Basal anterolateral S (%)	-22.76 ± 5.25	-25.75 ± 4.58	0.039*
Midanterolateral S (%)	-17.58 ± 6.11	-21.63 ± 5.14	0.036*
Basal inferoseptum S (%)	-20.42 ± 3.32	-23.21 ± 4.97	0.028*
Midinferoseptum S (%)	-20.54 ± 2.36	-22.11 ± 1.86	0.096
Basal anterior S (%)	-20.70 ± 6.33	-23.89 ± 7.10	0.044*
Midanterior S (%)	-18.81 ± 5.33	-22.07 ± 6.00	0.104
Basal inferior S (%)	-19.05 ± 6.18	-21.95 ± 7.41	0.210
Midinferior S (%)	-22.02 ± 3.12	-20.31 ± 4.22	0.102
Mean left ventricular S (%)	-20.02 ± 4.88	-22.82 ± 5.02	0.040*
Basal anterolateral SR (1/sn)	-2.30 ± 0.30	-2.40 ± 0.33	0.064
Midanterolateral SR (1/sn)	-1.85 ± 0.18	-2.07 ± 0.22	0.043*
Basal inferoseptum SR (1/sn)	-2.10 ± 0.43	-2.12 ± 0.32	0.034*
Midinferoseptum SR (1/sn)	-1.93 ± 0.24	-2.22 ± 0.11	0.076
Basal anterior SR (1/sn)	-2.19 ± 0.21	-2.57 ± 0.30	0.089
Midanterior SR (1/sn)	-2.18 ± 0.19	-2.26 ± 0.24	0.104
Basal inferior SR (1/sn)	-1.85 ± 0.16	-2.13 ± 0.32	0.029
Midinferior SR (1/sn)	-1.83 ± 0.22	-2.15 ± 0.28	0.107
Average left ventricular strain rate (1/sn)	-2.02 ± 0.24	-2.24 ± 0.26	0.026

* p< 0.05, statistical significance. S: Strain, SR: Strain rate.

In our study, the mean age of the AS group was 39.86 ± 9.38 years. In the AS group, the male to female ratio was 3.83. Considering that AS is 2-3 times more in men, our result is acceptable⁽¹⁷⁾. We did not find statistically significant differences in AS and control groups in terms of ventricular space diameters and wall thickness as in other studies⁽¹⁸⁻²⁰⁾. In our study, the left atrium diameter, which is one of the echocardiographic variables, was found to be larger in the AS group. In a study that investigated cardiac involvement in AS patients in 2000 years, similarly, the left atrium diameter was found significantly larger than the control group. They attributed this result to the fact that the first affected heart cavity in left ventricular diastolic dysfunction was the left atrium and AS caused diastolic dysfunction⁽²¹⁾. If we consider etiopathogenesis of diastolic dysfunction, this explanation seems reasonable. In our study, a statistically significant increase in right ventricular end-diastolic diameter was observed in the AS group.

Aortic involvement in AS is a life-threatening complication usually seen in late stages, but rarely seen in the early stage. Aortitis usually affects the aortic root and ascending aorta and often causes aortic insufficiency⁽²²⁾. Aortic valve involvement in AS usually causes inadequacy⁽²³⁾. In the study by Bergfeldt

et al., aortic insufficiency in 15%-20% of 91 patients was found to be the cause of AS⁽²⁴⁾. Qaiyumi et al. detected 4 AS and 3 Reiter syndrome cases in 100 aortic insufficiency patients⁽²⁵⁾. In a study by Roldan et al., 44 AS patients were examined with TEE. Subaortic hump was found in 74% of the patients and valve insufficiency (aortic or mitral) in 50%. During a 10-month follow-up, 24% of patients had new aortic root or valve involvement, and 12% recovered from existing abnormalities⁽²⁶⁾. Contrary to popular belief, aortic valve involvement appears to be quite common in AS. In our study, aortic valve involvement was found to be 17.24%. This value is in line with abovementioned study results. Compared to the control group, aortic valve involvement was statistically significantly higher (p= 0.039).

Diastolic functions in AS have been investigated by many researchers. In the study by Brewerton et al., which is an important study in understanding the pathophysiology of myocardial involvement in AS, diastolic functions were found to be significantly impaired⁽²⁷⁾. In another study by Çalışkan et al., A wave velocity and E/A ratio were found to be high at the limit, while mitral E wave velocity, DT, and IVRT were found to be significantly different than the control group⁽²⁸⁾. In the studies by Okan et al., diastolic dysfunction was detected in 6 AS patients

in conventional echo, while diastolic dysfunction was detected in 22 AS patients using TDI⁽²⁹⁾. In our study, diastolic dysfunction, E and A wave velocities, and DT from Doppler echo data of patients were similar in AS and control groups. Only IVRT in AS group was significantly prolonged ($p < 0.001$). There was no significant difference in lateral and septal mitral annulus S, E, and A wave velocities. While 7 patients (24.13%) in the AS group had impaired diastolic functions, there was no diastolic dysfunction in the control group and this difference was statistically significant. Although there was a significant difference between groups, diastolic dysfunction was slightly less common in our study than in other studies. This is attributed to the lower average age in the AS group and the long duration of the disease.

The importance of strain echo methods and their use in the evaluation of cardiac functions has recently increased. Strain measurements are generally taken by 2 methods (TDI strain and speckle tracking echo strain). Both methods have their own advantages and disadvantages, but they are both reliable in detecting myocardial damage⁽³⁰⁾. Although S and SR echo is not used as often as other echo methods, there are many potential uses in clinical practice. The ability of S echo to measure regional deformation according to segments directed attention to its use in ischemic heart diseases⁽¹³⁾. In a study of 97 patients with primary amyloidosis, the difference in TDI that could not be found with velocity imaging was detected using S and SR echo, which showed to be more sensitive. Even in patients without fractional shortening and heart failure, S and SR were able to distinguish echo⁽³¹⁾.

In our study, mean basal anterolateral, midanterolateral, basal inferoseptum, and basal anterior S values were significantly lower in AS than in control group. Midanterolateral, basal inferoseptum, basal inferior, and mean left ventricular SR values of the AS group were significantly lower than the control group. AS can disrupt systolic functions, both by increasing the frequency of ischemic heart disease and by the development of KMP secondary to inflammation. There is a need for further investigation of cardiac exposure in AS with new echocardiographic methods. We believe that S and SR echo may be useful in demonstrating subclinical myocardial dysfunction in AS. Our study is one of few studies on myocardial functions investigated by S and SR echocardiographic imaging methods in AS and it is original in this respect.

Limitations of the Study

Patients over 60 years old were not included in our study. We aimed to minimize the risk of developing cardiovascular diseases that adversely affect both diastolic and systolic functions. In this way, we planned to examine the pure AS effect as much as possible when evaluating cardiac functions, but this

is an important limitation of our study. We believe that the low number of patients and the short duration of their disease may cause inability to reveal possible cardiac function changes. In addition, taking echocardiographic measurements and ensuring image clarity was another limitation.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of the Afyonkarahisar Health Sciences University (Decision Number: 2019/222; Decision Date: June 17, 2019).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design – MT, AA; Analysis/Interpretation – ZY, MT; Data Collection – MT; Writing – ZY; Critical Revision – AA; Final Approval – MT, AA, ZY; Statistical Analysis – MT; Obtained Funding – MT; Overall Responsibility – ZY

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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