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Relationship between sacroiliitis and tricuspid annular plane systolic excursion in patients with ankylosing spondylitis

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ABSTRACT

Objectives: The study aimed to assess the association between sacroiliitis and tricuspid annular plane systolic excursion (TAPSE), a measure utilized to predict right ventricular systolic function in individuals with ankylosing spondylitis (AS).

Patients and methods: Demographic, clinical, laboratory, medical, and echocardiographic information of 90 AS patients (54 males, 36 females; mean age: 42.7±12.4 years; range, 23 to 72 years) between March 2018 and July 2023 was prospectively recorded. The patients were divided into two groups: those with normal (≥15 mm) TAPSE values (Group 1; n=69) and those with low (<15 mm) TAPSE values (Group 2; n=21). The groups were compared in terms of TAPSE values.

Results: In Group 2, the disease duration was longer (p=0.049), the use of tumor necrosis factor inhibitors was higher (p=0.046), and the rate of sacroiliitis was lower (p=0.012). Bath Ankylosing Spondylitis Disease Activity Index was higher in Group 2. In logistic regression analysis, there was an independent relationship between sacroiliitis in AS patients and Group 2 (odds ratio=0.088, 95% confidence interval: 0.008-0.960, p=0.046). Sacroiliitis had a close association with decreased right ventricular function in patients with AS.

Conclusion: There was an independent relationship between sacroiliitis and TAPSE in patients with AS.

Keywords: Ankylosing spondylitis, right ventricular function, tricuspid annular plane systolic excursion.

Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects and causes damage to axial and peripheral joints. It creates a significant health and socioeconomic burden on society.[1] Ankylosing spondylitis affects approximately 0.2 to 1.2% of the population and is 2.5 times more prevalent in males compared to females. Apart from joints, it most commonly causes anterior uveitis in the eyes and can also lead to significant organ damage in the cardiovascular system, lungs, kidneys, and nervous system.[2,3]

It is known that AS is not only due to aortic pathology but is also associated with cardiac complications such as left ventricular diastolic dysfunction, pericarditis, conduction disorders (atrioventricular or branch block), rarely mitral insufficiency, heart failure, and cardiomegaly.[4,5] Almost all patients with cardiac involvement are HLA (human leukocyte antigen)-B27 positive.[6,7] Mortality and morbidity are increased in AS patients with right ventricular (RV) cardiopulmonary disease. Tricuspid annular plane systolic excursion (TAPSE) is one of the noninvasive parameters used to evaluate the systolic functions of the RV and is known as the annular movement of the tricuspid valve in the normal heart. The normal TAPSE value is 15 to 20 mm. A TAPSE value <15 mm indicates RV dysfunction.[8,9] In AS patients, RV functions may be

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affected due to cardiac pathologies such as pulmonary arterial hypertension (PAH) and valve disease.[6,7] Hence, this study aimed to evaluate the relationship of TAPSE with sacroiliitis in AS patients.

PATIENTS AND METHODS

Ninety patients (54 males, 36 females; mean age: 42.7±12.4 years; range, 23 to 72 years) who visited the rheumatology clinic of the Recep Tayyip Erdoğan University Faculty of Medicine between March 2018 and July 2023 were enrolled in the cross-sectional prospective study. The patients were divided into two groups: those with normal TAPSE values (Group 1; n=69) and those with low TAPSE values (Group 2; n=21). The diagnosis of AS was determined according to the criteria outlined by the Assessment of Spondyloarthritis International Society.[10] Individuals under 18 years of age, individuals diagnosed with other rheumatological disorders, congestive heart failure, or severe valve disease, patients with a prosthetic heart valve, individuals with a history of lung disease, pulmonary hypertension, congenital heart disease, renal failure (estimated glomerular filtration rate <30 mL/min/1.7 m^2), or active infection, and patients with a history of malignancy were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdoğan University Faculty of Medicine Ethics Committee (date: 21.09.2023, no: 2023/220). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients' age, sex, body mass index, smoking status, comorbidities, and medication history were recorded. Disease duration was defined from the initial symptom onset. Laboratory tests were conducted on venous blood samples obtained from the patients following an 8-h fasting period. Complete blood count, serum creatinine, glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, C-reactive protein, and erythrocyte sedimentation rate were analyzed. Cigarette use was calculated in pack-years. Direct sacroiliac radiography and magnetic resonance imaging were conducted for sacroiliitis in patients presenting with inflammatory low back pain. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index were calculated for the participants.[11] Echocardiography was performed by the same experienced cardiologist.

Detailed two-dimensional transthoracic echocardiography was performed in all patients using Philips Epiq 7 with a 1 to 5 MHz X5-1 transducer (Philips Medical Systems Inc., Andover, MA, USA). Left atrial, left ventricular end-diastolic, and left ventricular end-systolic diameters and pulse and continuous Doppler measurements, E and A wave velocities, and deceleration time were quantified with standard two-dimensional M-mode echocardiographic images in accordance with current guideline recommendations.[13] Left ventricular ejection fraction was determined using the modified Simpson method. Left ventricular septal and posterior wall thicknesses were measured in the parasternal long axis view at the end of diastole. These measurements were used to calculate the left ventricular mass using the formula validated by Devereux et al.[12] left ventricular mass index=left ventricular mass/body surface area (body weight × 0.425 × height × 0.725 × 0.007184).[13,14]

Tricuspid annular plane systolic excursion was assessed as the complete excursion of the tricuspid annulus from its peak position after atrial contraction to its lowest point during ventricular systole, and TAPSE measurements were conducted in compliance with the most recent guidelines.[15] Patients with a TAPSE value ≥15 mm were considered to have a normal TAPSE and included in Group 1, while those with a TAPSE value <15 mm were considered to have decreased TAPSE and were included in Group 2.

Statistical analysis

The statistical analysis was performed using IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Numerical variables were presented as mean ± standard deviation (SD), while categorical variables were represented as percentages. Variables were evaluated for normal distribution through visual methods (histograms and probability plots) and analytical techniques (Kolmogorov-Smirnov/Shapiro-Wilk tests). To compare means between groups for normally distributed variables, the one-way analysis of variance was employed. Categorical variables were compared using either the chi-square test or Fisher exact test. Cross tabulations were used for comparison of the

TABLE 1
Demographic, medical, laboratory, and echocardiographic data of AS patients comparing Groups 1 and 2

	Group 1 (n=69)			Group 2 (n=21)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
	Demographic data						
Age (year)			43.1±12.4			41.7±11.1	0.671
Sex							
Male	45	65.2		9	42.9		**0.058**
BMI (kg/m^2)			27.9±5.1			26.7±4.5	0.379
Disease duration (year)			8.2±5.7			11.3±8.1	**0.049**
Diabetes mellitus	6	8.7		1	4.8		0.481
Hypertension	16	23.2		4	19		0.473
Hyperlipidemia	35	50.7		11	52.4		0.547
Smoking	29	42.6		8	38.1		0.457
BASDAI score			4.03±2.2			5±2.3	0.089
BASFI score			2.9±2.4			3.4±2.4	0.431
Uveitis	8	11.6		2	9.5		0.574
Peripheral arthritis	11	15.9		4	19		0.483
Lower back pain	67	97.1		20	95.2		0.554
Enthesitis	10	14.5		3	14.3		0.644
Dactylitis	2	2.9		1	4.8		0.554
Sacroiliitis	68	98.6		18	85.7		0.012
	Medical treatment						
Beta blocker	5	7.2		3	14.3		0.275
CCB	11	15.9		1	4.8		0.172
ACEI	7	10.1		2	9.5		0.650
ARB	7	10.1		1	4.8		0.400
Diuretics	11	15.9		3	14.3		0.580
Statins	5	7.2		1	4.8		0.572
OAD	3	4.3		1	4.8		0.662
NSAID	27	39.1		4	19.1		0.073
Anti TNF-α	40	58		17	81		0.046
IL-17A inhibitors	2	2.9		0	0		0.586
	Laboratory data						
WBC (×10^3/L)			7.8±2.5			7.7±1.8	0.811
HGB (g/L)			14±1.6			13.6±1.7	0.343
Glucose (mg/dL)			97.5±15.4			101.7±27	0.386
SCREA (mg/dL)			0.79±0.16			0.74±0.18	0.260
eGFR (mL/min/1.73 m^2)			105.1±16.5			107.3±14.1	0.560
HbA1c (%)			5.6±0.71			5.6±0.28	0.980
HLA B27 positive	36	52.9		13	61.9		0.321

TABLE 1
Continued

Variables	Group 1 (n=69) n	%	Mean±SD	Group 2 (n=21) n	%	Mean±SD	*p*
	Echocardiography data						
LVEF (%)			61.4±3.8			62.45.2	0.374
Mitral E wave			84.2±19.6			82.8±21.7	0.767
Mitral A wave			76.1±21.8			76.4±22.3	0.909
EA ratio			1.18±0.39			1.1±0.38	0.793
EE ratio			8.6±3.5			9.2±4.7	0.537
Deceleration time			206.1±57.3			195±52	0.389
LVMI (g/m^2)			81.3±24.4			82.5±30.5	0.857

SD: Standard deviation; BMI: Body mass index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CCB: Calcium channel blocker; ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blockers; OAD: Oral Antidiabetic Drugs; NSAID: Nonsteroidal Anti-inflammatory Drugs; TNF-α: Tumor necrosis factor-alpha; WBC: White blood count; HGB: Hemoglobin; SCREA: Serum creatinine; eGFR: Glomerular filtration rate; HbA1c: Hemoglobin A1C; HLA B27: Human leukocyte antigen B27; LVEF: Left ventricular ejection fraction; IL: Interleukin.

proportions of patients with categorical variables. After comparing the groups, the parameters were first evaluated with univariate logistic regression analysis to determine the predictors of Group 2, and the parameters found to be statistically significant as a result of this evaluation were evaluated with multivariate logistic regression analysis (enter method). A p-value <0.05 was considered statistically significant.

RESULTS

In Group 1, 11 patients had peripheral arthritis and 68 patients had sacroiliitis, while in Group 2, four patients had peripheral arthritis and 18 patients had sacroiliitis. A comparison of the data obtained between the two groups is presented in Table 1. In Group 2, disease duration was longer (p=0.049), anti-tumor necrosis factor use was higher (p=0.046), and sacroiliitis was lower (p=0.012). Although it did

TABLE 2
Investigating the relationship between sacroiliitis and decreased TAPSE values in AS patients using logistic regression analysis

Variables	Univaraite OR	95% CI Lower-upper	*p*	Multivariate OR	95% CI Lower-upper	*p*
Sex Male	0.400	0.148-1.083	0.071			
Disease duration	1.071	0.997-1.150	0.061			
Sacroiliitis	0.088	0.009-0.900	0.040	0.088	0.008-0.960	**0.046**
BASDAI score	1.212	0.969-1.516	0.092			
NSAID	0.366	0.111-1.205	0.098			
Anti TNF-α	3.081	1.103-10.123	0.032	3.086	0.901-10.570	0.073

TAPSE: Tricuspid annular plane systolic excursion; AS: Ankylosing spondylitis; OR: Odds ratio; CI: Confidence interval; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; NSAID: Nonsteroidal anti-inflammatory drugs; TNF-α: Tumor necrosis factor-alpha.

not reach statistical significance, the BASDAI score was higher in Group 2.

To determine the factors that predicted decreased TAPSE values in Group 2, univariate logistic regression analysis was performed using parameters that showed statistically significant differences between the groups (Table 2). Afterward, multivariate logistic regression analysis was performed using the parameters that remained significant in univariate analysis. As a result, we concluded that the presence of sacroiliitis in patients with AS had an independent association with Group 2 (odds ratio=0.088, 95% confidence interval 0.008-0.960, p=0.046). Sacroiliitis had a close association with decreased RV function in patients with AS.

DISCUSSION

Ankylosing spondylitis is a chronic inflammatory disease that leads to characteristic spinal deformities, such as flattening of lumbar lordosis and kyphosis, mainly as a result of axial involvement.[16] The inflammatory condition in the thoracic vertebrae and costovertebral joints gradually leads to fusion and ossification of the spine, resulting in increased dorsal kyphosis and thoracic stiffness.[17] Severe spinal kyphosis causes fatigue in the diaphragm and other muscles, intra-abdominal discomfort, and decreased lung function.[18] Decreased chest expansion and lung parenchymal abnormalities are significant factors linked to pulmonary dysfunction.[19]

Pulmonary arterial hypertension is more common in connective tissue autoimmune disorders such as systemic sclerosis, mixed connective tissue disease, and Sjögren's syndrome; however, there are limited studies on the association between ankylosing spondylitis and PAH. Inflammation and interstitial lung disease in connective tissue diseases are important mechanisms that play a role in the formation and progression of PAH. The risk of right heart failure and death is increased in these patients due to elevated pulmonary artery pressure. Pulmonary arterial hypertension symptoms in autoimmune diseases are nonspecific. Clinical evaluation, physical examination, respiratory function tests, echocardiographic measurements, and right heart catheterization are used in the diagnosis of PAH. In the study conducted by Colalillo et al.,[20] they reported that decreased TAPSE and TAPSE/systolic pulmonary artery pressure ratio in echocardiographic measurements in systemic sclerosis patients had predictive importance for the diagnosis of PAH and mortality.[21]

Studies have found a higher prevalence of death from cardiovascular disease in AS patients than the general population, particularly from congestive heart failure and ischemic heart disease.[22,23] In echocardiographic studies in AS, the prevalence of aortic valve insufficiency and diastolic left ventricular dysfunction was increased.[23,24] It has been suggested that the cause of left ventricular dysfunction may be impaired filling and relaxation of the left ventricle due to inflammation or fibrosis in the myocardium due to disease activity in AS patients.[22,23] While previous studies have examined left ventricular functions in AS patients, there is limited research on RV function in this population. In a study conducted by Karoli et al.,[25] echocardiography of 56 AS patients revealed PAH in 60.7%, RV dilatation in 30.4%, RV hypertrophy, and thickening of the interventricular symptoms in 37.5%. In this study, they found PAH to be common in AS patients. These changes were found to be correlated with thoracic spinal lesions and long disease duration. In another study on 55 AS patients with predominant spinal lesions, grade 3 sacroiliitis on plain radiographs, and long disease duration, PAH, RV hypertrophy, and RV dilatation were detected in 70.96%, 47.3%, and 34.5%, respectively.[26] There are cases in the literature describing the relationship between AS and PAH.[7,27] In our study, similar to previous literature, Group 2, which exhibited lower TAPSE values, had longer disease duration and higher disease activity scores. The longer duration of disease in Group 2, in which TAPSE was lower, may have caused changes in the myocardium over time. Excessive contraction of the myocardium may have caused a decrease in myocardial fibers over time and eventually led to the development of fibrosis. Myocardial fibrosis may also have caused a decrease in TAPSE. It has been demonstrated that RV fibrosis strongly correlates with RV function.[28] The value of RV fibrosis is still debated. Fibrotic remodeling may be a protective adaptation to some extent to preserve ventricular shape and function against increased pressures.[29] In AS, which is a chronic inflammatory disease, inflammation can increase myofibroblast activation, which may result in fibrosis.[30] Since patients who did not develop

pulmonary hypertension were included in this study, the increased TAPSE in patients with sacroiliitis might reflect an adaptive change that occurred in these patients in the early period.

In the lung, AS causes ankylosis in the thoracic vertebrae, fusion in the costovertebral joints, sternoclavicular joint, enthesitis in the manubrium, chest wall restriction, pleural thickening, apical fibrosis, and chest pain, causing difficulty in breathing and a decrease in respiratory functions. Additionally, obstructive sleep apnea syndrome is increased in these patients compared to the normal population. Pain in the waist and hips due to sacroiliitis and lumbar involvement are factors that affect lumbar flattening and breathing. Due to these changes, pressure increases in the pulmonary artery and RV functions are affected.[31] In our study, we found that TAPSE was increased in the group with sacroiliitis. It may suggest that there may be an increase in RV functions in patients with sacroiliitis to compensate for the decrease in lung capacity caused by pain or that it may be a finding due to pericardial involvement.

There are some limitations to this study. This single-center study involved a relatively small number of patients, which may limit the applicability of the results to a broader population. The limitations of the study include not using additional parameters and advanced imaging methods to assess the RV structure and functions in AS patients.

In conclusion, this is the first study to explore the correlation between sacroiliitis and TAPSE values in AS patients. This study found an independent relationship between sacroiliitis and TAPSE in patients with AS. Changes in cardiac function may occur in patients with AS without clinically significant myocardial damage. Transthoracic echocardiography, which is a noninvasive procedure to detect these functions at an early stage, can be used more frequently in daily practice.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Development of study concept and design: O.C.; Acquisition, analysis and interpretation of the data: E.E., O.C.; Statistical analysis: M.C.; Writing: O.C., K.I.

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