

Pulmonary Impairment Does Not Limit Exercise Capacity in Patients with Ankylosing Spondylitis with Low Disease Activity

Düşük Hastalık Aktivitesi Olan Ankilozan Spondilit Hastalarında Pulmoner Bozukluk Egzersiz Kapasitesini Sınırlamaz

Figen DAĞ,^a
 Özlem BÖLGEN ÇİMEN,^a
 Orhan GÜVENER,^a
 Gizem ERZURUMLUOĞLU,^a
 Didem OVLA ÇELİKCAN,^b
 Günşah ŞAHİN^a

Departments of

^aPhysical Medicine and Rehabilitation,

^bBiostatistics and Medical Information,

Mersin University Faculty of Medicine, Mersin

Received: 12.02.2018

Received in revised form: 03.04.2018

Accepted: 05.04.2018

Available online: 15.08.2018

Correspondence:

Figen DAĞ

Mersin University Faculty of Medicine,

Department of Physical Medicine and

Rehabilitation, Mersin,

TURKEY/TÜRKİYE

dagfigen@gmail.com

ABSTRACT Objective: To evaluate aerobic capacity and pulmonary function in patients with ankylosing spondylitis (AS) and compare these to the healthy controls and to investigate the possible relationship between aerobic capacity, pulmonary function and disease-specific measures. **Material and Methods:** Fourteen AS patients and 14 healthy controls were included in this prospective study. Clinical disease indices (BASDAI: Bath Ankylosing Spondylitis Disease Assessment Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: The Bath Ankylosing Spondylitis Metrology Index) were assessed. Participants completed questionnaires assessing physical activity level and quality of life. Aerobic capacity was assessed by submaximal treadmill test with breath-by-breath gas analysis. Aerobic capacity and pulmonary function tests were performed by an ergospirometry system. **Results:** The results of exercise tolerance test were similar in both groups (VO_{2max} for AS and control group; 40.03 ± 6.11 and 40.28 ± 4.54). AS patients had significantly lower vital capacity (VC) (4.42 ± 0.72 and 5.37 ± 0.72), and forced vital capacity (FVC) (4.36 ± 0.82 and 5.32 ± 0.71) and forced expiratory volume at first second (FEV1) (3.57 ± 0.74 and 4.20 ± 0.58) than healthy controls. Pulmonary function test results were not correlated with the disease duration, chest expansion and other clinical variables. In AS patients, only BASMI score showed significant association with FVC, FEV1, VC and chest expansion. No association between aerobic capacity and pulmonary function test variables, chest expansion, BASDAI, BASMI, BASFI was observed. There was no significant difference between groups in terms of physical activity level. Physical function, physical role limitations and bodily pain scores were significantly lower in AS group ($p < 0.05$). **Conclusion:** These results indicated that aerobic capacity in AS patients is not influenced by the reduced pulmonary function, probably due to the maintenance of an active life style.

Keywords: Ankylosing spondylitis; exercise test; quality of life

ÖZET Amaç: AS'li hastalarda aerobik kapasiteyi ve solunum fonksiyonlarını değerlendirmek ve bunları sağlıklı kontrollerle karşılaştırmak ve aerobik kapasite, pulmoner fonksiyon ve hastalığa özgü ölçümler arasındaki olası ilişkiyi araştırmak. **Gereç ve Yöntemler:** Bu prospektif çalışmaya 14 AS hastası ve 14 sağlıklı kontrol dahil edildi. Klinik hastalık endeksleri (BASDAI: Bath Ankylosing Spondylitis Hastalık Değerlendirme İndeksi, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index) değerlendirildi. Katılımcılar fiziksel aktivite düzeyini ve yaşam kalitesini değerlendiren anketler doldurdu. Aerobik kapasite, submaksimal koşu bandı testi ile değerlendirildi. Aerobik kapasite ve pulmoner fonksiyon testi bir ergospirometre sistemi ile gerçekleştirildi. **Bulgular:** Egzersiz tolerans testi sonuçları her iki grupta da benzerdi (AS ve kontrol grubu için VO_{2max} ; 40.03 ± 6.11 ve 40.28 ± 4.54). AS hastalarının vital kapasitesi (VK) (4.42 ± 0.72 ve 5.37 ± 0.72) ve zorlu vital kapasite (FVC) (4.36 ± 0.82 ve 5.32 ± 0.71) ve birinci saniyedeki zorlu ekspiratuvar hacim (FEV1) (3.57 ± 0.74 ve 4.20 ± 0.58) sağlıklı kontrollerden daha iyi idi. Akciğer fonksiyon test sonuçları ile hastalık süresi, göğüs ekspansiyonu ve diğer klinik değişkenler arasında korelasyon bulunmadı. AS hastalarında sadece BASMI skoru FVC, FEV1, VC ve göğüs ekspansiyonu ile ilişkiliydi. Aerobik kapasite ile solunum fonksiyon testi değişkenleri, göğüs ekspansiyonu, BASDAI, BASMI, BASFI arasında ilişki saptanmadı. Fiziksel aktivite açısından gruplar arasında anlamlı fark yoktu. Fiziksel işlev, fiziksel rol kısıtlılıkları ve vücut ağrısı skorları AS grubunda anlamlı olarak daha düşüktü ($p < 0.05$). **Sonuç:** Bu sonuçlar, AS hastalarında aerobik kapasitenin, muhtemelen aktif bir yaşam biçiminin devam etmesi nedeniyle akciğer fonksiyonlarının azalmasından etkilenmediğini ortaya koymuştur.

Anahtar Kelimeler: Ankilozan spondilit; egzersiz testi; yaşam kalitesi

Ankylosing spondylitis (AS) is a chronic, systemic, inflammatory rheumatic disease with unknown etiology among seronegative spondyloarthropathies. AS is often seen between 20-30 years and males are more often affected than females.¹ Clinically, it affects mainly the spinal column and sacroiliac joints and causes physical disability.² The main complaints of patients are pain, morning stiffness, fatigue and functional limitation, resulting with impairment in quality of life.³ The extra-articular manifestations in AS may include osteoporosis, uveitis, bowel disease, skin, kidney, cardiac and pulmonary involvement.

Cardiopulmonary abnormalities are well documented in patients with AS. Depending on the decrease in chest mobility, restrictive pulmonary deficiency, typically presented as restrictive pattern in pulmonary function test (PFT) has commonly been reported.^{4,5} Pulmonary function test in AS is generally characterized with reduced vital capacity [VC], reduced forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV_1) when FEV_1/FVC is normal.^{4,6,7} In patients with AS, aerobic capacity may be impaired by reduced pulmonary function due to the limited chest mobility, peripheral muscle weakness and deconditioning.⁵⁻¹⁰ Reduction in aerobic capacity compared to the healthy controls has been reported.^{6,9,11} However, there are also some literature that observed similar results of exercise tolerance test for both AS and healthy controls.^{7,12} Exercise tolerance test has become an important assessment tool in the evaluation of aerobic capacity. Maximal oxygen uptake (VO_{2max}) is accepted as the best index of aerobic capacity, and is assessed during a graded exercise test at open-circuit spirometry.⁶ Since VO_{2max} needs to attain a plateau in VO_2 as power output increases, using the term of VO_{2peak} instead of VO_{2max} has been recommended by Armstrong and Welsman [1997].¹³

The first aim of the study were to evaluate aerobic capacity and pulmonary function in patients with AS and to investigate whether exercise capacity is altered in correspondence to decline in pulmonary function. The second, compare these

parameters with healthy controls and also to investigate the possible relationship between aerobic capacity, pulmonary function and disease-specific measures.

MATERIAL AND METHODS

Fourteen AS patients and 14 age matched healthy controls (recruited from healthy hospital staff) with similar smoking status and physical activity level were eligible for inclusion in the study. Inclusion criteria consisted mainly of age >18 y, definite diagnosis of AS for at least 6 months according to the modified New York criteria, being sedentary for the six months prior to enrollment, male sex, and mental status sufficiently good to participation to the study. Study exclusion criteria included: [i] active peripheral joint involvement; [ii] Use of steroids in the last 6 months and treatment with beta-blockers; [iii] lower limb involvement that may interfered with exercise testing on the treadmill; [iv] presence of serious pulmonary, cardiac or endocrine diseases; [v] Any active infection that may affect the metabolic outcome of the exercise test, peripheral vascular disease, metabolic disease and other autoimmune, chronic systemic inflammatory disease. All participants were required to fill out a Physical Activity Readiness Questionnaire (PAR-Q), which assessed subject's readiness to participate to a physical activity.¹⁴ All subjects gave their written informed consent, which was approved by local ethics committee before testing commenced.

CLINICAL AND LABORATORIAL EVALUATIONS

All patients were in a steady phase of their disease and also all of them underwent a detailed physical examination. Disease duration, smoking history, current medicine usage, steroid treatment, usage of anti-TNF and duration of morning stiffness were recorded. Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) were assessed. The sacroiliitis was evaluated on antero-posterior sacroiliac joint radiography. Grading of sacroiliitis was performed according to the established scoring system.¹⁵ Height, weight, body mass index [BMI], chin-sternum sterni distance, tragus-to-

wall-distance, finger-to-floor distance, chest expansion, modified Schober index and intermalleolar distance were all measured by the same physician.

The Bath Ankylosing Spondylitis Metrology Index (BASMI) was used to assess axial mobility.¹⁶ BASMI is accepted as a standard index for establishing disease status and progression in patients with AS in terms of promptness, appropriateness and reliability. The BASMI consists of 5 objective measurements of the spinal column and the hip joints; cervical rotation, wall-tragus distance, lumbar lateral flexion, modified Schober's test and intermalleolar distance. Each examination reported either 0 point as a mild disease involvement, 1 point as a moderate disease involvement and 2 point as a severe disease involvement. Finally, it scores between 0-10 and the higher scores express as the more severe limitation of movement.

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to evaluate the disease activity.¹⁶ This index consists of 6 measurements of VAS that assess the 5 major symptoms of the disease consisting of fatigue, spinal and peripheral joint pain, sensitivity and morning stiffness. The average score of the two questions asked about the morning stiffness is calculated and collected with the other questions. The BASDAI score is obtained by converting the total value (0-50) to a scale of 0-10.¹⁶

Functional capacity was evaluated with Bath Ankylosing Spondylitis Functional Index (BASFI). This index consists of 8 questions about daily activities and 2 questions that evaluate the ability of patient to cope with daily life. Patients mark on the 10-cm VAS how difficult it is when doing the indicated tasks. By taking the average of the score obtained from 10 questions, the total score between 0-10 is calculated. Higher scores indicate more severe impairment.¹⁷

Physical activity levels of participants as MET (Metabolic Equivalent of Task)-min/week were identified using the long version of the last 7 days' self-administered International Physical Activity Questionnaire (IPAQ).¹⁸ Quality of life of partici-

pants was assessed by the Short Form 36 (SF-36). This questionnaire consists of 36 items measuring 8 dimensions: physical function, social function, physical role limitations, emotional role limitations, vitality, general health perceptions, bodily pain, and mental health and scored from 0 to 100 where higher scores indicate better health status.¹⁹

PULMONARY FUNCTION TEST

Pulmonary function tests were performed in all patients and healthy controls [Quark PFT, Cosmed Rome, Italy]. All of the participants were informed before the test and were allowed to sit upright with a nose clip attached in a comfortable, wheelless chair. The forced vital capacity (FVC, L), the forced expiratory volume at first second (FEV₁, L), FEV₁/FVC (%), maximum voluntary ventilation (MVV, L/min), maximal midexpiratory flow (FEF 25-75%) and vital capacity (VC, L) were recorded for every participant. The MVV was determined by the maximal voluntary ventilation over 12s. Spirometric measurements were done by the same physician in accordance with guidelines of American Thoracic Society and the European Respiratory Society (ATS/ERS).²⁰

CARDIOPULMONARY EXERCISE TEST

The cardiopulmonary exercise test was performed by the open-circuit spirometry (Quark PFT, Cosmed Rome, Italy). The metabolic analyzer was calibrated before each test with the 3 L calibration syringe and known gas calibration in line with the manufacturer's suggestion. Participants were instructed to refrain from food, caffeine and smoking within 3 hours of exercise test and not to perform any type of physical exercise on the test day. Before the cardiopulmonary test began, all participants walked for 10 min to familiarization for the treadmill.²¹ Submaximal exercise testing was performed on a treadmill ergometer according to modified Bruce protocol for estimating of VO_{2peak}. Submaximal exercise test is a valid and reliable physiological measurement for determining aerobic capacity.²² Inspired and expired gas samples was collected breath-by-breath through a face mask (Hans Rudolph, USA) during the test and data av-

eraging was performed after test finished using 30s average. The test was terminated when the participant reached at 85% of age predicted maximal heart rate (220-age) or subject could no longer continue exercising. The respiratory quotient (RQ) values of walking trials were also recorded to evaluate the intensity of the tests. Throughout the study protocol Borg scale with values ranging from 6 to 20 was applied at the end of every stage to assess participant's perceived exertion.²³

STATISTICAL ANALYSES

Descriptive statistics were presented as frequencies or mean±std deviation and median (25-75% percentiles) depending on whether the data were categorical or continuous. All continuous measurements were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk test. $P < 0.05$ was used to determine significance. As measurements did not display a normal distribution, non-parametric method Mann-Whitney U-test was used for independent groups' comparison. And independent-samples t test used to assess the parametric measures differences. Categorical data were compared using Pearson chi-square test. Correlation tests were performed using two-tailed Spearman (non-parametric) or Pearson [parametric] correlation coefficient. Statistical analysis was performed using the Statistical Package for Social Sciences, version 11.5 (SPSS, Inc., Chicago, IL) and MedCalc version 12.3.0. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the participants are summarized in Table 1. There are no statistically significant differences between groups with regard to age, body weight and smoking status ($P > 0.05$). Participants in AS group were significantly shorter than healthy controls, while BMI was not significantly different (30.25 (22.52-31.55) and 26.90 (23.80-30.02), respectively, ($P > 0.05$) (Table 1). Among 14 AS patients with disease duration of 5.32 (4.18) years sacroiliitis grades were observed with the following frequencies according to antero-posterior sacroiliac joint radiography:

grade 0 in 2 (14.3%), grade 1 in 2 (14.3%), grade 2 in 2 (14.3%), grade 3 in 4 (28.6%) and grade 4 in 4 patients (28.6%). Statistically significant difference was reached regarding chest expansion, tragus to wall distance, chin sternum distance and fingertip to floor distance between AS and control group, in favor of healthy controls (Table 1). There was no significant difference between groups in terms of physical activity level (AS group; 3090.00 (1893.00-5217.75) MET-min/week and control group; 4500.00 (3212.25-5643.00) MET-min/week, $p > 0.05$).

The results of the cardiopulmonary exercise test are summarized in the Table 2. Both groups completed the treadmill test in a similar duration ($p > 0.05$). There were no statistically differences between AS and control group with regard to VO_{2peak} , VCO_2 , respiratory quotient (RQ) and AT. All participants reached 85% or more of their age-predicted maximum heart rate (HR_{max}). HR_{max} was revealed also no statistically difference between groups (182.50 (178.00-187.25) and 180.00 (172.25-185.75), $P = 0.37$) (Table 2). At the end of the incremental treadmill test, rating of perceived exertion on the Borg scale was also similar in both groups (Table 2).

AS patients had significantly lower VC, FVC and FEV1 than healthy controls, whereas FEV1/FVC and other parameters related with pulmonary function test were similar (Table 2). These results indicate a restrictive type pulmonary impairment in the AS patients. Pulmonary function test results were not correlated with the disease duration, chest expansion and other clinical variables ($p > 0.05$). In AS patients, only BASMI score showed significant association with FVC ($r = -0.55$, $p = 0.039$), FEV1 ($r = -0.62$, $p = 0.017$), VC ($r = -0.54$, $p = 0.043$) and chest expansion ($r = -0.541$, $p = 0.046$). However, neither variables of the exercise test nor variables of pulmonary function test reported any statistically significant correlation with disease duration ($p > 0.05$). No association between aerobic capacity and pulmonary function test variables, modified Schober index, chest expansion, BASDAI, BASMI, BASFI were observed ($p > 0.05$).

Quality of life questionnaire (SF-36) scores of patients and controls are shown in Table 3. We

TABLE 1: Demographic and clinical characteristics of the participants.

	AS (n=14)	Controls (n=14)	P
Age (years)	32.71±5.94	30.86±6.64	0.44
Height (cm)	168.14±7.39	173.85±5.99	0.03*
Body weight (kg)	79.05±12.73	81.05±12.05	0.67
Smoking (yes/no)	9/5	10/4	0.13
ESR (mm/h)	8.57±7.00	N/A	
CRP (mg/L) ^b	6.76 (2.07-9.72)	N/A	
Disease duration (years)	5.32±4.18	N/A	
Pharmacology (%)			
Anti-TNF α	4 (28.6)		
NSAIDs	14 (100)		
Sulfasalazine	11 (78.6)		
Sulfasalazine + Anti- TNF α	4 (28.6)	N/A	
BASDAI	2.59±1.69	N/A	
BASFI	0.97±1.21	N/A	
BASMI	7.21±2.00	N/A	
Chest expansion	4.00±1.24	5.50±1.69	0.013*
Tragus to wall distance	16.50±3.32	9.07±3.29	<0.001*
Chin sternum distance ^b	1.00 (0.00-3.62)	0 (0-0)	0.006*
Finger to floor distance ^b	11.50 (3.87-29.00)	0 (0-3.25)	0<0.001*
Modified Schober	7.46±4.66	7.28±1.38	0.89
Intermalleolar distance	107.57±16.58	117.42±8.63	0.06

*Statistically significant differences ($P<0.05$). Values are reported as mean (\pm standard deviation) or number of participants (%), unless otherwise stated; ^b median percentiles (25-75). ESR: Erythrocyte sedimentation rate; CRP: C-Reactive protein; TNF: Tumor necrosis factor; NSAID: Non-steroid anti-inflammatory drug; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; N/A: Not applicable.

TABLE 2: Cardiopulmonary test results in ankylosing spondylitis and control groups.

Variable	AS (n=14)	Controls (n=14)	P
VO ₂ peak (mL/kg/min)	40.03±6.11	40.28±4.54	0.903
VO ₂ peak (mL/min)	3173.07±432.12	3266.86±503.42	0.601
VCO ₂ (mL/min)	3341.14±504.07	3422.57±538.13	0.683
RQ	1.05±0.05	1.06±0.04	0.711
AT (mL/kg/min)	29.75±5.01	31.14±6.08	0.516
Borg scale score	16.71±2.13	15.93±1.73	0.294
Time to exhaustion (min)	15.43±1.24	16.46±1.67	0.078
FEV ₁ (L)	3.57±0.74	4.20±0.58	0.019*
FVC (L)	4.36±0.82	5.32±0.71	0.003*
FEV ₁ /FVC (%)	81.67±5.43	79.15±5.61	0.239
VC (L)	4.42±0.72	5.37±0.72	0.002*
MVV (L/min)	124.85±28.81	137.16±28.24	0.264
FEF 25-75%	3.77±1.21	4.02±0.84	0.522

*Statistically significant differences ($P<0.05$). Values are reported as mean (\pm standard deviation). RQ: Respiratory quotient; FEV₁: Forced expiratory volume at first second; FVC: Forced vital capacity; VC: Vital capacity; MVV: maximum voluntary ventilation; FEF 25-75: maximal midexpiratory flow.

found that physical function, physical role limitations and bodily pain scores were significantly lower in AS group ($p<0.05$) (Table 3). There was no

association between SF-36 subgroups and VO_{2peak}, except physical function dimension ($r=0.384$, $p=0.022$).

TABLE 3: SF-36 scores of ankylosing spondylitis and control groups.

SF-36	AS (n=14)	Controls (n=14)	P
Physical function	85.00 [73.75-95.00]	95.00 [93.75-100.00]	0.004*
Social function	87.5 [62.5-100.0]	100 [84.37-100.00]	0.178
Physical role limitations	75.00 [43.75-100.00]	100 [100-100]	0.039*
Emotional role limitations	83.35 [33.30-100.00]	100 [66.7-100.0]	0.427
Bodily pain	61.50 [48.75-62.00]	84.00 [69.25-100.00]	0.006*
Vitality ^b	64.64±19.95	72.86±13.40	0.212
Mental health ^b	71.71±13.08	72.86±12.95	0.818
General health perceptions ^b	58.57±17.78	69.71±13.13	0.070

*Statistically significant differences ($P<0.05$) Median percentiles (25-75), unless otherwise stated; ^bMean (\pm standard deviation).

DISCUSSION

The main aim of this study was to investigate pulmonary function and aerobic capacity in patients with AS and compare these to the healthy controls. The results of pulmonary function test of present study are keeping in with previous studies, in which restrictive pattern are reported.^{4-9,24} Reduced FVC, FEV₁ and VC, but normal FEV₁ / FVC in patients with AS, suggest a restrictive defect in patients with AS. Hsieh et al. investigated 42 patients with AS and 42 healthy controls and found lower FVC, FEV₁ and TLC in AS group. Spinal mobility and chest expansion were also significantly limited in patients with AS.⁶ Despite stiffness of thorax and deformity of spinal column, limited movement of the chest wall, increased diaphragmatic contribution assists to maintain pulmonary ventilation.^{6,7} Seckin et al. reported that FVC and FEV₁ were significantly lower in the AS group; however FEV₁ / FVC were similar in both groups and reduction in chest expansion associated with pulmonary function test parameters but not with exercise tolerance.⁷ Fisher et al. hypothesized that limited chest expansion may affect VC and exercise capacity in patient with AS. They found that significant association between chest expansion and VC and exercise capacity was correlated with VC, but not with chest expansion. Consequently, they concluded that although limited chest expansion may lead to decline of VC, it's not a primary determinant of exercise capacity.²⁵

The reduction in chest expansion and reduced spinal mobility secondary to ankylosis of costover-

tebral and costosternal joints, cause respiratory abnormalities in patients with AS.^{4,26} In the present study, patients also had significantly lower chest expansion, vital capacity and aerobic capacity compared to healthy control group. However, no correlation was found between chest expansion and either pulmonary function or aerobic capacity. This is in contrast with other studies which have reported an association between chest expansion and restrictive pattern in pulmonary function tests.^{5,9,24}

The disease duration of AS patients in the present study was 5.32±4.18 years, therefore all patients were under medical treatment according to their disease status. Previous studies have different opinions whether disease duration related with pulmonary function in patient with AS or not. Many studies that reported an association between chest expansion and pulmonary function test parameters had patients who had a longer disease duration than ours; the mean disease duration ranged from 11.9 years to 22 years, while 5.32 years in the present study.^{5,4} Similar to our study, Tapia et al. and Maghraoui et al. studied with patients with shorter disease duration (8,4 years and 7.1 years, respectively) and found no correlation between chest expansion and pulmonary function test parameters.^{24,27} We observed that only the BASMI score was significantly correlated with FVC, FEV₁, VC and chest expansion. This result indicated that pulmonary function might be more associated with spinal mobility. It is also imported to improve inspiratory muscle performance for pulmonary function. Dragoi et al. has reported that inspiratory

muscle training improves aerobic capacity and pulmonary function in patients with ankylosing spondylitis.²⁸

Ozdemir et al. investigated whether reduced vital capacity affect the aerobic capacity of AS patients. They reported that AS patients have lower aerobic capacity and VO_2 peak was closely related with VC.⁵ Functional capacity and also aerobic capacity may be diminished in AS patients due to the musculoskeletal or pulmonary impairment.²⁹ It has been previously reported that patients with AS have decreased aerobic capacity.^{4,5,9} Many methods have been developed to evaluate aerobic capacity and to determine specific limiting factors. For this purpose, laboratory exercise tests are usually carried out on treadmill or bicycle ergometer. Relatively large range (7% to 24%) specified for VO_2 peak deficits in AS population. The diversity in VO_2 peak may be due to the different test protocols [treadmill vs. bicycles], estimating methods of VO_2 peak and participant characteristics.^{5,6,8,11} Our results identified that aerobic capacity in patients with AS was not significantly different than healthy controls. Both the AS and control groups achieved similar VO_2 peak. Since aerobic capacity is associated with diaphragmatic compensation and many other factors [peripheral muscle strength, cardiovascular condition, cardiopulmonary system etc.], patients with AS may have normal aerobic capacity despite reduced respiratory function, limited chest expansion and spinal mobility.^{8,25} Pulmonary impairment does not significantly limit aerobic capacity in this group of AS patients. This is in contrast to other studies which found a reduced VO_2 peak and also aerobic capacity in patients with AS.^{4,5,6,9} Hsieh et al. investigated 42 patients with AS and 42 sex- and age-matched healthy controls and found that AS group achieved a lower VO_2 peak than control group (21.8±5.1 vs. 25.1±5.7 mL/kg/min). They proposed that one of the causes of the low aerobic capacity in patients with AS might be cardiovascular pathologies.⁶ Since cardiovascular pathologies were among the exclusion criteria, patients with any cardiovascular disease were not included in our study. O'Dwyer et al. demonstrated that the predicted VO_{2max} was significantly lower

in the AS group than in the health control group and AS group had also significantly lower VO_2 peak at test condition.⁹ In another study of O'Dwyer et al. reported that aerobic capacity among the AS group was 24% lower than the control group.⁹ Similar results were specified by Carter et al. who studied with 20 patients with AS and 20 age and gender matched healthy controls. But this reduction in aerobic capacity was not related with respiratory muscle performance or reduced spinal mobility.⁸ Contrary to these findings, the results showed similar aerobic capacity in both AS and control group except for the Borg scale scores in Seckin et al. study.⁷ Likewise, well preserved aerobic capacity either expressed as maximal workload or as VO_2 peak was presented in study performed by van der Esch.¹² In both studies it's concluded that regular exercise or an active life style with maintenance of daily physical activity level is probably enough for the well-preservation of aerobic capacity in patients with AS.^{7,12} The overall well-preserved aerobic capacity of our subjects could be the result of an active life style. This is also supported by our physical activity survey results that not differed from healthy controls.

The BASFI has been demonstrated to be sensitive in evaluating functional capacity of patients with AS and it's considered that patients with a BASFI score ≥ 3 are more affected in functional capacity.³⁰ The mean BASFI score of AS patients in our study was 0.97±1.21. It was also indicated that AS patients with a BASFI score < 3 had a significantly better aerobic capacity than AS patients with a BASFI score ≥ 3 .⁶ Since BASFI contains the questions about daily activities and questions that evaluate the ability of patient to cope with daily life, patients who has BASFI score < 3 tend to have a better functional capacity. BASDAI has been used to evaluate the disease activity of patients with AS.¹⁶ Patients with a BASDAI score ≥ 4 are considered to have worse disease activity.^{31,32} High disease activity has been shown to be related with low levels of physical activity in patients with AS.³³ The mean BASDI score of AS patients in our study was 2.59±1.69. Hsieh et al. reported that patients with a BASDI score < 4 have better aerobic capacity than

those with a BASDAI score ≥ 4 .⁶ Both BASFI and BASDAI scores of our patients were found to be lower than the patients' scores in other studies.^{6,34} BASFI and BASDAI scores in our study may help to explain why there is no difference in aerobic capacity between patients and control group in our study.

Because of presence of various psychological symptoms such as pain, decreased functional ability, limited daily living activity it's considered that AS has negative effects on the quality of life.³⁵ Especially fatigue and pain symptoms have been recently shown as major factors that adversely affect the patient's quality of life.³⁶ Therefore, in health-related quality of life assessments, it is generally stated that physical parameters are more affected than social and mental aspects in patients with AS.³⁷ In the present study, physical function, physical role limitations and bodily pain dimension's scores were significantly lower in patients with AS than healthy controls. There was no association between SF-36 subgroups and VO_2 peak, except physical function dimension. Exercise and active life style have been shown to be effective in improving the quality of life.^{38,39}

In conclusion, our results show that submaximal exercise capacity in patients with AS is not affected although they have reduced pulmonary function. These results indicated that aerobic capacity in AS patients is not influenced by the diminished pulmonary capacity, probably due to the maintenance of an active life style.

The limitation of this study was that we had a relatively small number of AS patients and also matched healthy controls. Only male patients and controls subjects participated in the study to exclude the sexual metabolic differences. Further studies with more male and female patients and various disease activity scores may be planned to have detailed information about exercise capacity in AS patients. As different pharmacological agents have different effects on activity levels of

patients, our results might be affected by patients' medical treatment. Besides medical and conservative treatment, training of respiratory muscle, maintaining or improving spinal mobility and chest expansion, should be a part of a program for patients with AS. Patients also should be encouraged to have an active life style and to participate in regular exercise regimes to improve cardiorespiratory fitness.

Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Figen Dağ, Özlem Bölgen Çimen; **Design:** Figen Dağ, Özlem Bölgen Çimen, Didem Ovla Çelikcan; **Control/Supervision:** Figen Dağ, Özlem Bölgen Çimen, Günşah Şahin; **Data Collection and/or Processing:** Figen Dağ, Orhan Güvener, Gizem Erzurumluoğlu; **Analysis and/or Interpretation:** Figen Dağ, Günşah Şahin, Özlem Bölgen Çimen, Didem Ovla Çelikcan; **Literature Review:** Figen Dağ, Günşah Şahin, Özlem Bölgen Çimen; **Writing the Article:** Figen Dağ, Özlem Bölgen Çimen; **Critical Review:** Figen Dağ, Özlem Bölgen Çimen; **References and Fundings:** Figen Dağ, Günşah Şahin, Özlem Bölgen Çimen; **Materials:** Figen Dağ, Orhan Güvener, Gizem Erzurumluoğlu.

REFERENCES

- Braun J, Sieper J. Ankylosing spondylitis. *Lancet* 2007;369(9570):1379-90.
- Aytekin E, Caglar NS, Ozgonenel L, Tutun S, Demiryontar DY, Demir SE. Home-based exercise therapy in patients with ankylosing spondylitis: effects on pain, mobility, disease activity, quality of life, and respiratory functions. *Clin Rheumatol* 2012;3(1):91-7.
- Lim HJ, Moon YI, Lee MS. Effects of home-based daily exercise therapy on joint mobility, daily activity, pain, and depression in patients with ankylosing spondylitis. *Rheumatol Int* 2005;25(3):225-9.
- Berdal G, Halvorsen S, van der Heijde D, Mowe M, Dagfinrud H. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study. *Arthritis Res Ther* 2012;14(1):R19.
- Ozdemir Yr O, Inanici F, Hasçelik Z. Reduced vital capacity leads to exercise intolerance in patients with ankylosing spondylitis. *Eur J Phys Rehabil Med* 2011;47(3):391-7.
- Hsieh LF, Wei JC, Lee HY, Chuang CC, Jiang JS, Chang KC. Aerobic capacity and its correlates in patients with ankylosing spondylitis. *Int J Rheum Dis* 2014;19(5):490-9.
- Seçkin U, Bölükbaşı N, Gürsel G, Eröz S, Sepici V, Ekim N. Relationship between pulmonary function and exercise tolerance in patients with ankylosing spondylitis. *Clin Exp Rheumatol* 2000;18(4):503-6.
- Carter R, Riantawan P, Banham SW, Sturrock RD. An investigation of factors limiting aerobic capacity in patients with ankylosing spondylitis. *Respir Med* 1999;93(10):700-8.
- O'Dwyer T, O'Shea F, Wilson F. Decreased health-related physical fitness in adults with ankylosing spondylitis: a cross-sectional controlled study. *Physiotherapy* 2015;102(2):202-9.
- Köseoglu F, Ozel S, Demirdaviren S, Karabiyikoglu G, Yorgancioglu. Effects of a pulmonary rehabilitation program on pulmonary functions, cycle ergometry test parameters, exercise tolerance and spinal mobility in patients with ankylosing spondylitis. *European Journal of Physical Medicine and Rehabilitation* 1998;8:67-70.
- Halvorsen S, Vøllestad NK, Fongen C, Provan SA, Semb AG, Hagen KB, et al. Physical fitness in patients with ankylosing spondylitis: comparison with population controls. *Phys Ther* 2012;92(2):298-309.
- van der Esch M, van't Hul AJ, Heijmans M, Dekker J. Respiratory muscle performance as a possible determinant of exercise capacity in patients with ankylosing spondylitis. *Aust J Physiother* 2004;50(1):41-5.
- Armstrong N, Welsman JR. *Young People & Physical Activity*. 1st ed. Oxford: Oxford University Press Medical Publications; 1997. p.26-9.
- Thomas S, Reading J, Shephard RJ. Revision of the physical activity readiness questionnaire (PAR-Q). *Can J Sport Sci* 1992;17(4):338-45.
- van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27(4):361-8.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21(12):2286-91.
- Karatepe AG, Akkoc Y, Asar S, Kirazli Y, Akkoc N. The Turkish versions of the Bath Ankylosing Spondylitis and Dougados functional indices: reliability and validity. *Rheumatol Int* 2005;25(8):612-8.
- Booth M. Assessment of physical activity: an international perspective. *Res Q Exerc Sport* 2000;71(2 Suppl):S114-20.
- Koçyiğit H, Aydemir Ö, Fisek G, Ölmez N, Memiş AK. [Reliability and validity of Turkish version of (SF-36)]. *İlaç ve Tedavi Dergisi* 1999;12(2):102-6.
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al; ATS/ERS Task Force. Standardisation of spirometry. *Eur Respir J* 2005;26(2):319-38.
- Ford MP, Wagenaar RC, Newell KM. Arm constraint and walking in healthy adults. *Gait Posture* 2007;26(1):135-41.
- Noonan V, Dean E. Submaximal exercise testing: clinical application and interpretation. *Phys Ther* 2000;80(8):782-807.
- Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14(5):377-81.
- Brambila-Tapia AJ, Rocha-Muñoz AD, Gonzalez-Lopez L, Vázquez-Del-Mercado M, Salazar-Páramo M, Dávalos-Rodríguez IP, et al. Pulmonary function in ankylosing spondylitis: association with clinical variables. *Rheumatol Int* 2013;33(9):2351-8.
- Fisher LR, Crawley MI, Holgate ST. Relation between chest expansion, pulmonary function and exercise tolerance in patients with ankylosing spondylitis. *Ann Rheum Dis* 1990;49(11):921-5.
- Sampaio-Barros PD, Cerqueira EM, Rezende SM, Maeda L, Conde RA, Zanardi VA, et al. Pulmonary involvement in ankylosing spondylitis. *Clin Rheumatol* 2007;26(2):225-30.
- El Maghraoui A, Chouair S, Abid A, Bezza A, Tabache F, Achemlal L, et al. Lung findings on thoracic high-resolution computed tomography in patients with ankylosing spondylitis. Correlations with disease duration, clinical findings and pulmonary function testing. *Clin Rheumatol* 2004;23(2):123-8.
- Drăgoi RG, Amaricai E, Drăgoi M, Popoviciu H, Avram C. Inspiratory muscle training improves aerobic capacity and pulmonary function in patients with ankylosing spondylitis: a randomized controlled study. *Clin Rehabil* 2016;30(4):340-6.
- Karapolat H, Eyigor S, Zoghi M, Akkoc Y, Kirazli Y, Keser G. Are swimming or aerobic exercise better than conventional exercise in ankylosing spondylitis patients? A randomized controlled study. *Eur J Phys Rehabil Med* 2009;45(4):449-57.
- Davis JC Jr, Van Der Heijde D, Braun J, Dougados M, Cush J, Clegg DO, et al. Recombinant human tumor necrosis factor receptor (etanercept) for treating ankylosing spondylitis: a randomized, controlled trial. *Arthritis Rheum* 2003;48(11):3230-6.
- Cohen JD, Cunin P, Farrenq V, Oniankanta O, Carton L, Chevalier X, et al. Estimation of the Bath Ankylosing Spondylitis Disease Activity Index cutoff for perceived symptom relief in patients with spondyloarthropathies. *J Rheumatol* 2006;33(1):79-81.
- Zochling J. Measures of symptoms and disease status in ankylosing spondylitis. *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S47-58.
- Fongen C, Halvorsen S, Dagfinrud H. High disease activity is related to low levels of physical activity in patients with ankylosing spondylitis. *Clin Rheumatol* 2013;32(12):1719-25.
- Dagfinrud H, Kvien TK, Hagen KB. The Cochrane review of physiotherapy interventions for ankylosing spondylitis. *J Rheumatol* 2005;32(10):1899-906.
- Bostan EE, Borman P, Bodur H, Barça N. Functional disability and quality of life in patients with ankylosing spondylitis. *Rheumatol Int* 2003;23(3):121-6.
- Durmuş D, Alaylı G, Uzun O, Tander B, Cantürk F, Bek Y, et al. Effects of two exercise interventions on pulmonary functions in the patients with ankylosing spondylitis. *Joint Bone Spine* 2009;76(2):150-5.
- Casserty IP, Fenlon HM, Breatnach E, Sant SM. Lung findings on high-resolution computed tomography in idiopathic ankylosing spondylitis--correlation with clinical findings, pulmonary function testing and plain radiography. *Br J Rheumatol* 1997;36(6):677-82.
- Fernández-de-Las-Peñas C, Alonso-Blanco C, Alguacil-Diego IM, Miangolarra-Page JC. One-year follow-up of two exercise interventions for the management of patients with ankylosing spondylitis: a randomized controlled trial. *Am J Phys Med Rehabil* 2006;85(7):559-67.
- Karapolat H, Akkoc Y, Sari I, Eyigor S, Akar S, Kirazli Y, et al. Comparison of group-based exercise versus home-based exercise in patients with ankylosing spondylitis: effects on Bath Ankylosing Spondylitis Indices, quality of life and depression. *Clin Rheumatol* 2007;27(6):695-700.