

Original Article

A Possible Correlation Among Different Disease Activity Parameters and Functional Status in Patients with Ankylosing Spondylitis

Ankilozan Spondilitli Hastalarda Farklı Hastalık Aktivite Parametreleri ve Fonksiyonel Durum Arasındaki Muhtemel İlişki

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Objectives: The primary aim of this study was to assess the possible relationship among the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), and two Ankylosing Spondylitis Disease Activity Score (ASDAS) including the C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) scores in patients with ankylosing spondylitis (AS). The secondary aim was to investigate gender differences in terms of disease activity scores and functional status.

Patients and methods: Five hundred patients (158 females, 342 males; mean age 37.2±9.9 years; range 15 to 70 years) with AS were enrolled. Disease activity was assessed through the BASDAI, ASDAS-CRP and ASDAS-ESR, while functional status was evaluated by the BASFI.

Results: The mean BASDAI, ASDAS-CRP, ASDAS-ESR, and BASFI scores were 3.71±2.26, 1.65±0.83, 2.59±1.12, and 2.68±2.38, respectively. The BASDAI and ASDAS-ESR values of the female patients with AS were significantly higher than those of the males. The BASDAI and BASFI were significantly associated with the two ASDAS scores. According to the BASDAI, 46.6% of the patients had a high disease activity and had significantly higher values in terms of symptom duration, compared to those with lower BASFI, and two ASDAS scores. The ASDAS-CRP scores of the disease activity indices were similar in both genders.

Conclusion: Our study results suggest that the two ASDAS scores are significantly associated with the disease activity and functional status. We believe that using ASDAS-CRP indices is more suitable for a disease activity parameter in further studies involving patients with AS in both genders, however not analyzing gender differences.

Key words: Ankylosing Spondylitis Disease Activity Score; Ankylosing spondylitis; Bath Ankylosing Spondylitis Disease Activity Index; disease activity; gender.

Amaç: Bu çalışmanın birincil amacı, ankilozan spondilitli (AS) hastalarda Bath Ankilozan Spondilit Hastalık Aktivite İndeksi (BASDAI), Bath Ankilozan Spondilit Fonksiyonel İndeksi (BASFI) ve C-reaktif protein (CRP) ve eritrosit sedimentasyon hızını (ESH) içeren iki Ankilozan Spondilit Hastalık Aktivite Skoru (ASDAS) arasındaki muhtemel ilişkiyi araştırmaktır. İkincil amacı ise, hastalık aktivitesi ve fonksiyonel durum açısından cinsiyet farklılıklarını araştırmaktır.

Hastalar ve yöntemler: Çalışmaya AS'li 500 hasta (158 kadın, 342 erkek; ort. yaş: 37.2±9.9 yıl; dağılım 15-70 yıl) alındı. Hastalık aktivitesi BASDAI, ASDAS-CRP ve ASDAS-ESH ile değerlendirilirken, fonksiyonel durum BASFI ile değerlendirildi.

Bulgular: Ortalama BASDAI, ASDAS-CRP, ASDAS-ESH ve BASFI skoru sırasıyla 3.71±2.26, 1.65±0.83, 2.59±1.12 ve 2.68±2.38 idi. Ankilozan Spondilitli kadın hastaların BASDAI ve ASDAS-ESH değerleri, erkek hastalara kıyasla, anlamlı olarak daha yüksekti. BASDAI ve BASFI skorları, iki ASDAS skoru ile anlamlı düzeyde ilişkili bulundu. Hastaların %46.6'sı, BASDAI skoruna göre yüksek hastalık aktivitesine sahipti ve bu hastalarda hastalık süresi, BASFI ve ASDAS skorları düşük olanlara kıyasla, anlamlı olarak daha yüksekti. Hastalık aktivite indekslerinden ASDAS-CRP skorları her iki cinsiyettede benzerdi.

Sonuç: Çalışma bulgularımız, iki ASDAS skorunun hastalık aktivitesi ve fonksiyonel durum ile ilişkili olduğunu göstermektedir. Ankilozan spondilitli hastalarda ASDAS-CRP indeksinin her iki cinsiyeti içeren ancak cinsiyet farklılıklarına ilişkin analiz yapılmayacak ileriki çalışmalarda, hastalık aktivite parametresi olarak kullanılmasının daha uygun olacağı kanısındayız.

Anahtar sözcükler: Ankilozan Spondilit Hastalık Aktivite Skoru; ankilozan spondilit; Bath Ankilozan Spondilit Hastalık Aktivite İndeksi; hastalık aktivitesi; cinsiyet.

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Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that predominantly occurs in the sacroiliac joints and the spine and manifests with pain, joint stiffness, and loss of spinal mobility.[1] This chronic, progressive inflammatory disease results in substantial functional limitations and affects several aspects of the patient's life, such as psychological status and quality of life (QoL). It is important to follow-up patients with AS regularly to determine the best therapeutic approach. In clinical practice, measurement tools are used for regular patient monitoring and assistance with making treatment decisions in AS.[2] The most commonly used instrument for disease activity is the self-administered Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire since it is quick and simple to complete. The BASDAI includes the whole spectrum of AS symptoms related to fatigue, swelling, pain, and morning stiffness,[3] but it is a subjective measurement that exclusively reflects the patient's perspective. [4] It has been reported that self-reported assessment tools, such as the BASDAI, may be influenced by a patient's psychological status.^[5] As a result of the limitations of BASDAI, the Ankylosing Spondylitis Disease Activity Score (ASDAS) instrument, which includes both selfreported domains and objective measures, was also developed to assess disease activity in patients with AS.[3,6,7] Four ASDAS versions have been evaluated, and the one that includes total back pain, peripheral pain/ swelling, duration of morning stiffness, the patient's global assessment of disease activity, and C-reactive protein (ASDAS-CRP) was selected by members of the Assessment of Spondyloarthritis international Society (ASAS) as the preferred version. [7] If the ASDAS-CRP is not available, then the ASDAS version with erythrocyte sedimentation rate (ASDAS-ESR) can be used as an alternative.[7,8]

Functional status is an important outcome parameter in patients with AS in order to monitor disease effects. The Bath Ankylosing Spondylitis Functional Index (BASFI) is a valid instrument that can be utilized to measure physical function in patients with AS, one of the ASAS core elements that was recommended to be measured when following up AS patients. The BASFI can also be used to evaluate disease response to therapy using the ASAS response criteria.

The prevalence and clinical presentation of AS differs between genders. In spite of a male predominance, the male-to-female ratio for AS was recently reported to be approximately 2–3:1.^[11] In addition, reports have shown that women with AS

have higher disease activity according to the BASDAI as well as higher fatigue levels. [12] Furthermore, they reportedly have more peripheral arthritis and more self-reported functional limitations. [13] Men and women may have a different phenotype of AS that may affect the clinical course, time to diagnosis, and treatment choices. [13] Therefore, identifying gender differences in patients with AS in terms of disease activity scores and functional status can influence the choice of treatment.

The primary aim of this study was to assess the relationship between the BASDAI, BASFI, and two ASDAS scores in patients with AS. The secondary aim was to investigate the gender differences in terms of disease activity scores and functional status.

PATIENTS AND METHODS

Five hundred patients (158 females, 342 males; mean age 37.2 \pm 9.9 years; range 15 to 70 years) were enrolled in this retrospective, cross-sectional study and were diagnosed according to the modified New York criteria for the diagnosis of AS. [14] They were recruited from the Physical Medicine and Rehabilitation Department of Rheumatology outpatient clinics of two hospitals. Both clinics follow-up patients with AS regularly and record their demographic and disease-related variables. For the present study, a cross-sectional analysis was conducted only on patients with available baseline data. Those taking tumor necrosis factor alpha (TNF- α) blockers were not included in the study. In addition, the local ethics committee approved the study.

The demographic and clinical variables, including gender, age, duration of symptoms, and medications [non-steroidal anti-inflammatory drugs (NSAIDs); disease-modifying antirheumatic drugs (DMARDs)] the patients were using, had been recorded beginning from the first patient visit, and this information was obtained from the hospital files. The BASDAI, ASDAS-ESR, and ASDAS-CRP were calculated and recorded to assess disease activity. The BASDAI consists of six questions concerning fatigue, spinal pain, joint pain or swelling, areas of localized tenderness, pain severity, and duration of morning stiffness, and the patients answer the questions on a 10 cm visual analog scale (VAS). Lower scores indicate less active disease.[3,15] The ASDAS-ESR and ASDAS-CRP are deduced using formulas that were chosen by the ASAS group, [6,7] and the scores are then calculated with the answers from questions 2, 3, and 6 on the BASDAI, the patient's global assessment of disease acitivity, and the CRP (mg/l) for the ASDAS-CRP or ESR (mm/h) for the ASDAS-ESR.^[7]

Table 1. Demographic and clinical characteristics of the patients with ankylosing spondylitis

		All patients					Male					Female				
	n	%	Mean±SD	Median	Minmax.	n	%	Mean±SD	Median	Minmax.	n	%	Mean±SD	Median	Minmax.	p
Age (years)*			37.2±9.9	36	15-70			36.9±9.8	35	15-64			37.8±10.1	37	17-70	0.334
Duration of																
symptoms (years)*			7.5±7.1	5	0.3-46			7.9 ± 7.7	6	0.5-46			6.4±5.7	4.5	0.3-28	0.077
NSAID usage	438	87.6				297	87.1				140	88.6				0.643
DMARD usage	393	78.6				270	79.2				122	77.2				0.608
BASDAI*			3.7 ± 2.3	3.72	0-9.38			3.4 ± 2.2	3.3	0-9.38			4.3 ± 2.2	4.4	0-9.3	< 0.001
ASDAS-CRP*			1.6 ± 0.8	1.7	0-4.4			1.6 ± 0.9	1.65	0-4.4			1.7 ± 0.8	1.7	0-3.5	0.428
ASDAS-ESR*			2.6±1.1	2.5	0-15			2.5±1.2	2.35	0.4-15			2.8±0.9	2.7	0-6.4	0.002
BASFI*			2.7 ± 2.4	2.16	0-9.8			2.6±2.4	2.1	0-9.8			2.9 ± 2.3	2.39	0-9.6	0.109

^{*} Data is expressed as mean ± standard deviation and median (minimum-maximum); NSAID: Non steroidal anti-inflammatory drug; DMARD: Disease modifying anti-rheumatic drug; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C-reactive protein levels; ESR: Erythrocyte sedimentation rate; BASFI: Bath Ankylosing Spondylitis Functional Index.

The functional status of the patients in our study was evaluated with the BASFI. This instrument consists of 10 questions. Eight of them are about daily activities and two assess the patients' ability to cope with everyday life. As with the BASDAI, the patients answer the questions using a 10-cm VAS. Higher scores on the BASFI indicate more severe impairment.^[9,16]

In this study, statistical analysis was performed with the SPSS version 11.0 for Windows software program (SPSS Inc., Chicago, IL, USA), and the descriptive data was presented as mean \pm standard deviation (SD). The demographic characteristics were compared using a chi-square test, and the Mann-Whitney U test was used for comparisons between the two genders. Any correlations that existed between the BASDAI, ASDASCRP, ASDAS-ESR, and BASFI were investigated using the Spearman test because the variables did not show normal distribution. A p value of less than 0.05 was considered to be statistically significant.

RESULTS

The demographic and clinical characteristics of the patients with AS are shown in Table 1. There were significant differences between the male and female patients with this disease according to the BASDAI and ASDAS-ESR, with the values of the female patients being significantly higher than those of the male patients (p<0.05).

The correlations between the two ASDAS scores and the BASDAI and BASFI in the AS patients are shown in Table 2. The BASDAI and BASFI were positively correlated with the ASDAS-CRP and ASDAS-ESR, and the BASDAI was also positively correlated with the BASFI in both the male and female patients with AS (r=0.689 and r=0.668 respectively, p<0.001). The ASDAS-CRP was also found to be positively correlated with the ASDAS-ESR in the same two groups of patients (r=0.846 and r=0.841 respectively, p<0.001).

The demographic and clinical variables of the AS patients according to disease activity using the BASDAI for classification are shown in Table 3. Low disease activity was represented by a BASDAI score of <4 and high disease activity as a score of ≥4. According to this instrument, 233 (46.6%) of the AS patients had high disease activity, and these had significantly higher values in terms of duration of symptoms, the BASFI, and the two ASDAS scores.

Table 2. Correlations between the two ASDAS scores, BASDAI, and BASFI

	Male p	atients	Female patients			
	ASDAS-CRP	ASDAS-ESR	ASDAS-CRP	ASDAS-ESR		
BASDAI						
r	0.753	0.674	0.740	0.645		
Р	0.000	0.000	0.000	0.000		
BASFI						
r	0.585	0.548	0.578	0.476		
P	0.000	0.000	0.000	0.000		

r: Correlation coefficient; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C-reactive protein levels; ESR: Erythrocyte sedimentation rate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

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Table 3. Demographic and	clinical variables of patients	s with low or high disease a	activity according to the BASDAI

]	Patients with l	ow disease	activity	I						
		(BA	SDAI <4)								
	n	Mean±SD	Median	Minmax.	n	Mean±SD	Median	Minmax.	Р		
Number of patients	267				233						
Males	203				138						
Females	64				94						
Age (years)*		36.52±9.52	35	17-64		37.88±10.19	37	15-70	0.125		
Duration of symptoms											
(years)*		6.81±7.19	4	0.3-46		8.18±6.98	6	0.3-40	0.003		
BASDAI*		1.97±1.23	2	0-3.96		5.72±1.30	5.52	4-9.38	< 0.001		
BASFI*		1.38±1.49	0.8	0-7.1		4.18 ± 2.32	4.14	0-9.8	< 0.001		
ASDAS-CRP*		1.18 ± 0.64	1.2	0-2.8		2.19 ± 0.69	2.2	0.12-4.4	< 0.001		
ASDAS-ESR*		2.06 ± 0.77	2.1	0-5		3.19±1.15	3.2	1.1-15	< 0.001		

^{*} Data is expressed as mean ± standard deviation and median (minimum-maximum); BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C-reactive protein levels; ESR: Erythrocyte sedimentation rate.

DISCUSSION

The ASDAS was developed as a validated, highly discriminatory index for assessing disease activity in patients with AS. While the BASDAI includes patient-reported assessments, the ASDAS also includes laboratory parameters.^[7] In this study, we investigated the relationship between the BASDAI, the two ASDAS scores, and the BASFI in AS patients and found that the two ASDAS scores were significantly correlated with the BASFI and BASDAI. Furthermore, the BASDAI and ASDAS-ESR levels of the female patients were significantly higher than the male patients, but the ASDAS-CRP levels of the two genders were similar. The BASDAI also revealed that 46.6% of the AS patients had active disease, and these also had significantly higher values in terms of duration of symptoms, the BASFI, and the two ASDAS scores.

The female patients had significantly higher values of disease activity on the BASDAI than their male counterparts in our study. Additionally, previous studies that investigated gender differences in patients with AS reported higher disease scores on the BASDAI^[12,17] as well as higher values of fatigue,^[12,17] peripheral joint pain,^[17] and local tenderness^[12,13,17] in female patients.

Fibromyalgia (FM) is a condition characterized by chronic widespread pain and tender points, and patients with this condition further complain of a wide variety of symptoms, including fatigue.^[18] It has been reported that FM is more prevalent in female patients with AS, and it has also been found to be correlated with the BASDAI and BASFI.^[19,20]

Azevedo et al.^[20] reported that six out of 17 women in their study had FM, whereas only five out of 54 men were afflicted. Aloush et al.[19] reported that half of the women with AS had concomitant FM; however, none of the men had this condition. Additionally, there was a significant correlation between the higher BASDAI and BASFI scores and FM in past studies.[19,20] The fatigue levels and local tenderness of patients with AS who have concomitant FM is expected to be high. Some patients may also report higher levels of disease activity and lower functional status depending on their psychological profile.^[5] In light of our research, the higher BASDAI values in the female patients in this study may be the result of higher levels of fatigue and local tenderness or concomitant FM. However, we did not evaluate fatigue and local tenderness individually. Moreover, because this study was retrospective in nature, the concomitant FM and the psychological profiles of the patients were also not evaluated.

While the ASDAS includes the categories of spinal pain, peripheral joint pain, morning stiffness, the patient's global assessment of disease activity, and laboratory parameters, [21-23] it does not include fatigue and local tenderness. The ASDAS-ESR levels of the female patients in this study were significantly higher than those of the male patients, but the ASDAS-CRP levels for both genders were similar. Tests to determine ESR values are frequently ordered in clinical medicine because they are simple to perform and inexpensive. Many factors affect ESR, for example gender, the menstrual cycle, obesity, age, anemia, infection, and drug therapy, but females seem to have higher levels. [24]

Because we were not able to investigate these factors in this retrospective study, we could not determine which of them affected the ESR levels of our subjects. Taking into consideration these findings, the ASDAS-CRP appears to be a more convenient instrument than the ASDAS-ESR for measuring disease activity in female patients with AS.

Previous studies have reported significantly higher BASFI scores in patients with AS who have high disease activity compared with those exhibiting low disease activity, and [25,26] our findings were consistent with these results. The BASFI score was higher in the group with BASDAI scores of \geq 4, and it was significantly correlated with the BASFI. In addition, the two ASDAS scores were also correlated with the functional status of the patients.

Conclusion

In this retrospective study, the scores on the ASDAS-CRP and ASDAS-ESR, including both the self-reported items and the objective measures, were significantly correlated with disease activity and functional parameters. Of the disease activity indices, there were no differences in the ASDAS-CRP scores between the males and females. Furthermore, the ASDAS-ESR and the BASDAI scores of the female AS patients were higher than for the males. Regarding future studies involving AS patients that will include both genders but not include an analysis of gender differences, we believe that the ASDAS-CRP score is a better choice for assessing disease activity parameters. However, future longitudinal studies are still needed to investigate the differences between genders and to determine the most appropriate indices for evaluating disease activity, functional status, and response to therapy in patients with AS.

Declaration of conflicting interests

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