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ORIGINAL ARTICLE

Association of work instability with fatigue and emotional status in patients with ankylosing spondylitis: comparison with healthy controls

Yasemin Ulus[1] · Yesim Akyol[1] · Ayhan Bilgici[1] · Omer Kuru[1]

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Abstract

Introduction/Objective Ankylosing spondylitis (AS) is usually seen in among younger person of working age and carries a significant economic burden. It was aimed to explore the relation of work instability with fatigue, depression, and anxiety in working AS patients comparing with healthy controls.

Method This case-control study was conducted on working 61 AS patients and 40 sex-age-matched working healthy controls. The data were collected using Visual analogue scale-pain, Bath AS Disease Activity Index, Bath AS Functional Index, Bath AS Metrology Index in patients; and Beck Depression Inventory, Beck Anxiety Inventory, Multidimensional Assessment of Fatigue, AS Work Instability Scale in all participants. Data were analyzed by SPSS, using chi-squared test, Mann–Whitney *U* test, Kruskal–Wallis test, Spearman correlation analysis, and multivariate linear regression analysis.

Results Depression, fatigue, and work instability scores were significantly higher in patients than controls ($p < 0.05$). Clinical parameters (except spinal mobility) showed a significant worsening across the levels of work instability in patients ($p < 0.05$) and work instability scores were positively correlated with all clinical parameters except spinal mobility ($p < 0.001$). There was a weak correlation between work instability and spinal mobility ($p < 0.05$). Fatigue ($p < 0.001$), pain, and functional capacity scores ($p < 0.05$) were found to be influential variables on work instability scores.

Conclusion The results of this study demonstrated that fatigue and depressive symptoms had negative effect on work instability beside pain, disease activity, and functionality in patients with AS. The recognition and improvement of fatigue and depression may lead to reduced risk of job loss in these patients.

Keywords Ankylosing spondylitis · Anxiety · Depression · Fatigue · Work

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease that involves the axial skeleton, the enthesis, and the peripheral joints. Men have a higher risk of symptomatic disease than women with a sex ratio of 2–3:1 [1]. The onset of AS is usually in among younger person of working age. AS carries a significant economic burden arising from indirect costs associated with loss of earnings and reduced productivity, as well as direct healthcare costs [2]. It is important to identify the limitations or difficulties in the workplace experienced by the patients with AS during their working years [3].

Work instability represents the consequences of a mismatch between persons' functional abilities and the demands of their job, and if it is not well identified, continuing employment may be threatened [3]. Work instability reflects the difficulties in meeting job requirements from person's perspective and informs about the person's job productivity [2, 4]. In patients with AS, work instability has been investigated in limited number of studies [2, 4–7]. In these studies, the association of work instability with disease activity and quality of

✉ Yasemin Ulus
yaseminulus@gmail.com

Yesim Akyol
yesimakyol@yahoo.com

Ayhan Bilgici
abilgici@omu.edu.tr

Omer Kuru
omeromu@gmail.com

[1] Department of Physical Medicine and Rehabilitation, Medical Faculty, Ondokuz Mayis University, Samsun, Turkey

life was shown. It was reported that loss of productivity was associated to a higher impairment of quality of life and presence of emotional problems [4].

To the best of our knowledge, the relationship between the work instability and fatigue, depression, and anxiety has not been studied in patients with AS before. In this study, the aim was to explore the relation of work instability with fatigue, depression, and anxiety in working AS patients comparing with healthy controls.

Methods

Participants

Actively working 61 patients with AS who fulfilled the modified New York Criteria [8] attending the Department of Physical Medicine and Rehabilitation of Medical Faculty of Ondokuz Mayıs University were assessed at the outpatient clinic between January 2017 and February 2018. Forty sex-age-matched working healthy controls who met inclusion criteria and agreed to participate to the study were also enrolled in this case-control study. Interventions with controls recruited from general population (university employees, relatives of patients from outpatient-inpatient clinics, healthy volunteers) were carried out by the same physician (YU) as in patients. Exclusion criteria were having concomitant diseases or disorders that might affect their work status, other rheumatic diseases, and severe somatic or psychiatric disorders. None of the participants was receiving psychiatric treatment including psychotherapy or antidepressants, etc. The study protocol was approved by the Medical Research Ethics Committee at Ondokuz Mayıs University (B.30.2.ODM.0.20.08/1410) and verbal consent was obtained from participants.

Measures

All participants were questioned about age, number of education years completed, work type (sedentary/manual) and duration, medical comorbidities, and smoking habits. Patients were also asked whether they left the previous job because of AS. Disease duration, family history, current medications, and laboratory evaluations including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were reported in patients. Patients completed a 10-cm visual analogue scale (VAS) for pain (0 = no pain, 10 = very severe pain) [9].

Disease-related variables

Data about disease-related variables including disease activity measured by the Bath Ankylosing Spondylitis Disease Activity Index [10] and functional capacity measured by the Bath Ankylosing Spondylitis Functional Index [11] were recorded in patients. These indexes with higher values indicate worse disease activity and worse function, respectively [12, 13]. Scores of spinal measurements of the patients were calculated by using Bath Ankylosing Spondylitis Metrology Index (BASMI) conducted by a physician (YU). It includes the measurements of wall to tragus distance, lumbar flexion, cervical rotation, lumbar lateral flexion, and intermalleolar distance [14].

Emotional status

Emotional status of the all participants was assessed by Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) [15, 16]. The BDI consists of 21 questions about how the subject has been feeling in the last week and gathers information on different symptoms of depression. Each item on the scale is scored from 0 to 3. It provides information both about the presence and the severity of depression, on somatic, emotional, cognitive, and motivational dimensions. Higher scores imply the presence of more depression [17]. The BAI is a brief measure of anxiety with a focus on somatic symptoms of anxiety. It has a total of 21 items. Respondents indicate how much they have been bothered by each symptom over the past week. Reponses are rated on a 4-point Likert scale and range from 0 to 3 [18]. Higher scores of these scales show increased depression and anxiety of subjects.

Fatigue

Fatigue level of the participants was evaluated by Multidimensional Assessment of Fatigue (MAF) [19]. This scale contains five dimensions of fatigue within the past week: degree, severity, distress, impact on activities of daily living, and timing. Each 100-mm VAS was converted to a 10-point numerical rating scale. The scores range from 0 (no fatigue) to 50 (severe fatigue) [20].

Work instability

The Ankylosing Spondylitis Work Instability Scale (ASWIS) is a disease-specific questionnaire to assess work instability on patient self-perceived impact of disease on work. It is a self-administered simple 20-item questionnaire scored from 0 to 20 (0 = no risk, 20 = maximum risk of work instability) and was adapted to Turkish by Kucukdeveci et al. [5, 7]. This scale was administered to all participants and patients were classified as having no risk if ASWIS score was 0–10 (group 1), as having moderate risk if ASWIS score was 11–17 (group 2), and as having high risk if ASWIS score was 18–20 (group 3) [5].

Table 1 Comparison of demographic and clinical characteristics of the patients with ankylosing spondylitis and controls

Characteristics	Patients ($n = 61$) Median (minimum–maximum) 95% CI (lower bound-upper bound)	Controls ($n = 40$) Median (minimum–maximum) 95% CI (lower bound- upper bound)	p
Age	40 (19–57) 36.79–41.01	39.5 (21–61) 35.63–41.87	0.906
Years of education (years)	8 (5–16) 8.32–10.33	11 (5–15) 9.57–11.73	0.100
Work duration (years)	18 (1–40) 14.73–19.31	13 (1–40) 11.31–17.14	0.670
BDI score (0–63)	7 (1–26) 5.72–8.05	4(0–25) 3.42–6.53	0.004*
BAI score (0–63)	1 (0–44) 2.22–5.88	0 (0–11) 0.88–2.87	0.073
MAF score (0–50)	26.7 (0–42.1) 19.202–25.700	1 (1–42.9) 3.025–8.861	<0.001*
ASWIS score (0–20)	11 (2–20) 9.09–11.79	2 (0–16) 2.73–3,76	<0.001*
0–10 no risk (n, %)	30, % 49.2		
11–17 moderate risk (n, %)	24, % 39.3		
18–20 high risk (n, %)	7, % 11.5		
Disease duration (years)	7 (1–28) 6.99–10.27	–	–
ESR (mm/h)	7 (1–28) 8.38–15.39	–	–
CRP (mg/l)	0.4 (0.01–11.3) 0.3852–1.2234	–	–
VAS pain score (0–10)	4 (0–8) 3.63–4.70	–	–
BASDAI score (0–10)	2.4 (0–7.2) 2.198–2.926	–	–
BASFI score (0–10)	0.5 (0–5) 0.671–1.222	–	–
BASMI score (0–10)	1 (0–6) 1.39–2.11	–	–
	n (%)	n (%)	
Medication use			
Biological agents	57 (93.4)	–	–
DMARDs	16 (26.2)		
Corticosteroid	1 (1,6)		
NSAIDs	27 (44.3)		
Gender			
Female	7 (11.5)	9 (22.5)	0.168
Male	54 (88.5)	31 (77.5)	
Work type			
Sedentary	17 (27.9)	10 (25)	0.821
Manual	44 (72.1)	30 (75)	
Smoking	25 (41.0)	16 (40.0)	0.942

CI confidence intervals, *BDI* Beck Depression Inventory, *BAI* Beck Anxiety Inventory, *MAF* Multidimensional Assessment of Fatigue, *ASWIS* Ankylosing Spondylitis Work Instability Scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *VAS* visual analogue scale, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *BASMI* Bath AS Metrology Index, *DMARDs* disease-modifying anti-rheumatic drugs, *NSAIDs* non-steroidal anti-inflammatory drugs

*p value is significant when <0.05

Statistical analyses

The data were analyzed using the IBM SPSS version 22.0 for Windows. The sample size was calculated by a statistician with PASS 2011 software. A priori power analysis using data from a previous study [21] assessing fatigue in AS indicated that a sample of 60 patients and 40 controls would have 0.98 power and $p < 0.01$ based on MAF scores. The Kolmogorov-Smirnov test was used to analyze normal distribution assumption of the quantitative outcomes and all data were not normally distributed. Descriptive data were presented as minimum–maximum (median). The sociodemographic characteristics of the patients and controls were compared by chi-squared test. Mann–Whitney U test was used to compare

clinical parameters of patients and controls. Kruskal–Wallis test and post hoc analysis (Mann–Whitney *U* test) were used to compare the parameters in three groups of patients according to their ASWIS scores. The correlations were investigated by using Spearman correlation analysis. Multivariate linear regression analysis was performed to determine if VAS pain, BDI, BAI, BASDAI, BASFI, and MAF scores were associated with ASWIS scores.

Results

The sample consisted of 61 patients aged between 19 and 57 years and 40 healthy controls aged between 21 and 61 years. Demographic and clinical characteristics of the participants are shown in Table 1. There was no significant difference with regard to demographic characteristics (age, gender, years of education, smoking) among patients and controls ($p > 0.05$). Work duration and working type were not different in patients and controls ($p > 0.05$). On the other hand, BDI, MAF, and ASWIS scores were significantly higher in patients than controls ($p < 0.05$) (Table 1).

Table 3 Correlation coefficients between the clinical parameters in patients with ankylosing spondylitis ($n = 61$)

	BDI	BAI	MAF	ASWIS
VAS pain	0.302*	0,356*	0.423*	0.517**
BDI	–	0.716**	0.442**	0.601**
BAI	0.716**	–	0.416*	0.585**
BASDAI	0.441**	0.477**	0.659**	0.608**
BASFI	0.428*	0.320*	0.384*	0.563**
BASMI	0.197	0.140	0.217	0.280*
MAF	0.442**	0.416*	–	0.649**

VAS visual analogue scale, *BDI* Beck Depression Inventory, *BAI* Beck Anxiety Inventory, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *BASMI* Bath AS Metrology Index, *MAF* Multidimensional Assessment of Fatigue, *ASWIS* Ankylosing Spondylitis Work Instability Scale

*$p < 0.05$

**$p < 0.001$

Of the patients 9 (14.8%) reported that they quitted the previous job because of AS. One-third of the patients (31.1%) had positive family history and 14 (23%) had

Table 2 Comparison of the clinical parameters in the patients according to work instability risk

Characteristics	Group 1 (ASWIS:0–10) ($n = 30$)	Group 2 (ASWIS:11–17) ($n = 24$)	Group 3 (ASWIS:18–20) ($n = 7$)	p*
	Median (min–max)	Median (min–max)	Median (min–max)	
Age (years) [b]	38 (27–57)	39.5 (19–49)	44 (38–47)	0.137
Years of education (years) [c]	11 (5–16)	6.5 (5–15)	8 (5–8)	0.113
Work duration (years)	18 (2–40)	18 (1–32)	20 (10–30)	0.879
Disease duration (years)	7 (1–28)	7.5 (2–24)	6 (2–21)	0.7525
ESR (mm/h)	5 (2–41)	8.5 (1–69)	8 (5–30)	0.485
CRP (mg/l)	0.3 (0.01–4.5)	0.4 (0.01–11.)	0.4 (0.01–0.82)	0.689
VAS pain score (0–10) [a, c]	3 (0–8)	5 (2–8)	7 (2–8)	0.002
BDI score (0–63) [b, c]	4 (1–14)	7 (1–11)	11 (9–26)	< 0.001
BAI score (0–63) [a, b, c]	0 (0–6)	2 (0–14)	17 (7–44)	< 0.001
BASDAI score (0–10) [a, b, c]	1.7 (0–4.4)	2.9 (1.2 ± 5.7)	4 (2.4–7.2)	< 0.001
BASFI score (0–10) [a, b, c]	0.3 (0.0–1.6)	0.8 (0.0–2.7)	2.5 (1–5)	< 0.001
BASMI score (0–10)	1 (0–5)	1.5 (0–5)	2 (1–6)	0.128
MAF score (0–50) [a, b, c]	15.2 (1.0–38.6)	29.1 (13–41)	34.9 (25.1–42.1)	< 0.001

ASWIS Ankylosing Spondylitis Work Instability Scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *VAS* visual analogue scale, *BDI* Beck Depression Inventory, *BAI* Beck Anxiety Inventory, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *BASMI* Bath AS Metrology Index, *MAF* Multidimensional Assessment of Fatigue

*Kruskal–Wallis test

[a] Significant difference between group 1 and group 2 with Mann–Whitney *U* test

[b] Significant difference between group 2 and group 3 with Mann–Whitney *U* test

[c] Significant difference between group 1 and group 3 with Mann–Whitney *U* test

Table 4 Multiple regression analysis with ASWIS as dependent variable and VAS pain, BDI, BAI, BASDAI, BASFI, and MAF as independent variables ($n = 61$)

	Work instability (ASWIS)				
	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. error	β	t	p
Pain (VAS)	0.780	0.307	0.303	2.542	0.014*
Depression (BDI)	0.220	0.149	*0.191*	1.473	0.147
Anxiety (BAI)	0.054	0.092	0.073	0.587	0.560
Disease activity (BASDAI)	−0.756	0.593	−0.201	−1.275	0.208
Function (BASFI)	1.643	0.511	0.331	3.216	0.002*
Fatigue (MAF)	0.169	0.045	0.408	3.735	0.000*

*p value is significant when <0.05

comorbidities (4 with hyperlipidemia under control with diet and 10 with controlled hypertension). None of the comorbidities was associated with fatigue and had any effect on work status. Of the patients 57 (93.4%) were receiving biologic agents.

Table 2 provides the comparison of demographic and clinical parameters in patients according to their ASWIS scores. Clinical parameters (except BASMI) were significantly different in the three groups ($p < 0.05$) (Table 2). VAS pain scores in group 2 and BDI scores in group 3 were significantly higher than the other groups ($p < 0.05$) (Table 2).

In correlation analysis, the demographic and laboratory parameters were not correlated with clinical findings ($p > 0.05$). There were strong positive correlations between ASWIS sores and BDI, BASDAI, and MAF scores ($p < 0.001$) (Table 3). ASWIS scores were also correlated with VAS, BAI, and BASFI moderately ($p < 0.001$) (Table 3).

The relationship between ASWIS scores and clinical parameters according to multivariate linear regression analysis are shown in Table 4. It has been found that the most significant correlation with ASWIS scores was MAF scores ($p < 0.001$) (Table 4). VAS pain and BASFI scores were also found to be influential variable on ASWIS scores ($p < 0.05$) (Table 4).

Discussion

In the present study, the work instability in working AS patients was higher than controls. The main determinants of work instability were found to be pain intensity, fatigue, and depressive symptoms. The impact of AS on work status can be seen in various aspects of workforce participation, from requiring more assistance at work to withdrawal from the workforce [3, 22, 23]. It is a known fact that unemployment and withdrawal from the workforce for patients with AS were higher than in general population [22]. Fabreguet et al. found that work instability was high in spondyloarthritis [6]. In the current study; although almost half of the patients had no risk for work instability, ASWIS scores were significantly higher in working AS patients than controls ($p < 0.001$). It seems that patients with AS were experiencing more mismatches at work when compared to the age-gender-matched individuals whose work duration and work type were similar with patients. In a study Barlow et al. [24], of the patients with AS, 15% reported that they had to change their working lives attributable to AS (reduction in hours worked, change of job). Similarly, the percentage of quitting previous job because of AS was 14.8% in our study.

Fatigue is one of the major symptoms in AS and is related to clinical and functional status, health-related quality of life, and psychiatric symptoms [21, 25, 26]. It is considered as the third most disabling domain after stiffness and pain [27]. In clinical trials, tumor necrosis factor (TNF) inhibitor therapy has been shown to improve fatigue in patients with AS [28]. On the other hand, Wu et al. reported the limited effect of anti-TNF treatment for fatigue [29]. In the present study, although most of the patients were on biologic therapy, they reported more fatigue than controls. Fatigue is associated with work disability and contributes to work productivity impairment in patients with AS [23, 24, 30]. In a single-cohort qualitative study, patients reported that fatigue contributed towards early retirement or a change in employment [31]. In the current study, strong relationship was found between MAF and ASWIS scores and the most important determinant of work instability was fatigue ($p < 0.001$). MAF scores showed a significant worsening across the levels of work instability. These results demonstrate once more that the fatigue is important symptom to be taken into account in working AS patients. The early determination of fatigue may reduce the risk of work instability and ensure that essential precautions are taken before job loss in working AS patients.

Patients with AS are at increased risk for psychological distress and they are more likely to suffer from depression and anxiety when compared to the healthy individuals and the general population [32–34]. In previous studies, depression and anxiety were found to be related to work disability in patients with AS [22–24]. Although

Frauendorf et al. reported that presence of emotional disturbance was associated with loss of work productivity in patients with AS [4], there is no study evaluating the relationship between work instability and emotional status in these patients. In the current study; although depression level of the patients with AS were not found to be very high, patients reported more depressive symptoms than controls ($p < 0.05$). On the other hand, anxiety scores were similar in both groups. The increase in risk of job loss was correlated with more anxious and depressive mood in patients with AS ($p < 0.001$). It can be stated that anxiety and depression should not be ignored in working AS patients. The presence of emotional problems should be explored as soon as possible, before a job loss occurs in these patients.

Sociodemographic and disease-related factors (such as disease duration, pain, disease activity, function) are also related to work performance in patients with AS. It was shown that older age, poor function, longer disease duration, and higher disease activity were influential factors on work status [22, 23, 35]. In the literature, there are only three studies that evaluated the relationship between work instability and disease related factors. In these studies ASWIS scores were significantly correlated with BASDAI and BASFI. Fabreguet et al. [6] have assessed the work instability in spondyloarthritis and they have found that patient's global assessment was the main determinant of work instability. In the current trial, VAS pain, BASDAI, and BASFI scores were significantly different between the patients who had no risk, had moderate, and had high risk of job loss according to ASWIS scores. The correlation between the work instability and disease activity was strong, and work instability was moderately correlated with pain and functionality ($p < 0.001$). On the other hand, pain and function were the major determinant of work instability ($p < 0.05$). These results were in line with previous studies and indicated that AS patients with higher disease activity and pain intensity, and with poor function might have higher risk of job loss. Unlike previous studies, sociodemographic characteristics such as age, disease duration, work type, and work duration of the patients had no effect upon work status in our study.

In a review by Gobelet et al., it was stated that severe lumbar movement restriction, limitation of cervical rotation, and hip disease were related to work disability [36]. In the current study, spinal mobility was assessed by BASMI. It reflects the axial status of patients with AS. BASMI scores did not differ between ASWIS risk groups and there was a weak correlation between BASMI and ASWIS scores. It can be said that mobility may not be as important in work status as other disease-related parameters. On the other hand, it should be noted that the AS sample in our study had a good mobility with a median BASMI score of 1 (0–6). Since there is no study evaluating the relationship between work instability and mobility, future studies including patients with mobility restriction may clarify this issue.

This study was limited with cross-sectional design so direction or causality of the correlations could not be inferred. Additionally, since the results belong to single center, they could not be generalized to broader population. There is lack of evidence about the impact of fatigue and emotional status on work instability. Our study may be as a model to the future studies on work instability in patients with AS. Lastly, AS patients in this study had a median BASDAI score of 2.4 indicating mildly active disease [12]. This may be due to the fact that a great majority of the patients (93.4%) were on biologic agents. This is an unavoidable result due to the increasing use of biologic therapy recently. This will be clarified by the studies to be performed in biologic agent naive patients. On the other hand; despite the mild disease activity, it seems that fatigue and depressive symptoms have negative impact on work instability in patients with AS. Given the small number of women in our sample (11.5%), we were unable to draw any conclusion about gender differences in work instability. Since AS is more commonly diagnosed in men, an imbalance in sex distribution can be expected. Future studies involving larger number of women with AS may be planned for this respect.

If the factors affecting work status are well defined, appropriate clinical or work place intervention will maintain the work continuity and productivity in AS patients [5]. Work instability is defined as an indicator for the level of risk of the inability to work due to health problems [3]. When considered from this aspect, the results of this study are important for demonstrating the negative effect of fatigue and depressive symptoms in work instability beside pain, disease activity, and functionality in patients with AS. The early recognition of fatigue and depressive symptoms may lead to reduced risk of job loss in these patients. It may be beneficial to design targeted interventions to improve fatigue and psychological health in working AS patients.

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Yesim Akyol: Contributions to the conception, interpretation of data for the work, revising the work critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work.

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Compliance with ethical standards

Disclosures None.

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