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The status and correlation factors of fatigue in patients with ankylosing spondylitis (FACIT-F): a cross-sectional study based on the Chinese population

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Abstract

Objective To analyze the status and correlation factors of fatigue in patients with ankylosing spondylitis (AS), and provide a reference for improving the fatigue status of patients with AS.

Method Using the AS-specific disease database of the Chinese Rheumatology Registration and Research Information Platform, patients with AS from 9 centers in China were selected as study subjects from March 2022 to September 2023. Functional Assessment of Chronic Illness Therapy Scale (FACIT-F) score, AS disease activity score-C-reactive protein (ASDAS-CRP), AS disease activity score-erythrocyte sedimentation rate (ASDAS-ESR), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Function Index (BASFI), Bath Ankylosing Spondylitis Measurement Index (BASMI), Patient Global Assessment (PGA) score, night pain score, Depression Anxiety Stress Scale (DASS-21) and AS International Community Health Index Assessment (ASAS-HI) were observed. Human leukocyte antigen B27 (HLA-B27), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of the patients were detected. The data were analyzed by Spearman correlation and multiple linear regression.

Result A total of 338 patients with AS were included in this study. Spearman correlation analysis results of 338 AS patients with fatigue showed that age, disease course, ASDAS-CRP, ASDAS-ESR, BASDAI, PGA, BASFI, BASMI, ASAS-HI and so on were the main correlation factors of fatigue ($P < 0.05$); Multiple linear regression analysis showed that BASDAI, ASAS-HI, depression and so on were independent predictors of fatigue in AS patients ($P < 0.05$). Spearman correlation analysis of no or very mild fatigue group showed that age, ASDAS-CRP, ASDAS-ESR, BASDAI, BASFI, ASAS-HI and so on were the main correlation factors of fatigue ($P < 0.05$); Multiple linear regression analysis showed that age, BASDAI, ASAS-HI were the independent predictor of fatigue in AS patients ($P < 0.05$). Spearman correlation analysis in the mild and moderate fatigue group showed that ASDAS-CRP, BASDAI, PGA, BASFI, ASAS-HI and so on were the main

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factors influencing fatigue ($P < 0.05$); Multiple linear regression analysis showed that BASDAI, depression and stress were independent predictors of fatigue in AS patients ($P < 0.05$).

Conclusion In this study, fatigue was obvious in 37.9% of AS patients, and patients' fatigue levels were closely related to disease activity (ASDAS, BASDAI and PGA) and psychological factors (anxiety, depression and stress). At the same time, the higher the degree of fatigue, the more obvious the impact of disease activity and psychological factors on fatigue.

Keywords Ankylosing spondylitis, Fatigue, FACIT-F, Disease activity, Psychological factors

Ankylosing spondylitis (AS) is a chronic progressive autoimmune disease. As a refractory autoimmune disease worldwide, the prevalence rate of AS in China was about 0.3% [1]. In recent years, fatigue in AS patients has received more and more attention from scholars at home and abroad. A cross-sectional study from China found that the incidence of fatigue in patients with AS was 48.7% [2]. Modern clinical research shows that pain, morning stiffness and fatigue are the three most common symptoms of AS patients when they go to the doctor, among which fatigue is considered to be the main systemic symptom, at the same time, fatigue is one of the important factors leading to poor efficacy, decline in quality of life and even disability in AS patients [3]. Studies have shown that moderate and severe fatigue is an independent risk factor affecting the quality of life of patients with AS, and appropriate intervention for fatigue, can significantly improve the quality of life [4]. Some scholars suggest that fatigue should be used as an important indicator to evaluate the clinical outcome of AS patients, and that fatigue should be part of routine clinical evaluation [5].

Fatigue is a complex subjective experience. People with the disease describe fatigue as fatigue at rest, fatigue during activities, lack of energy that interferes with daily work, inertia or lack of stamina, or loss of vitality. In rheumatic immune diseases, fatigue is defined as "a persistent subjective feeling of systemic lethargy and fatigue." [6]. Fatigue, as a specific subjective feeling, can be quantified by fatigue scores and fatigue indicators and can be modified according to the underlying causes of fatigue through a variety of measures, including complex interactions between social, demographic, biological, disease-related and behavioral processes [5, 7]. A Turkish study estimated that fatigue occurs in more than half of patients with AS, significantly affects affecting work, family, daily activities, mood and cognition, and significantly reduces the quality of life of patients with AS [8]. A longitudinal observational cohort from Canada showed that patients with AS who were severely fatigued tended to have higher disease activity scores, along with increased acute phase proteins and a significant decrease in quality of life [9]. Fatigue in AS patients has been found to be associated with quality of life, functional ability, and depression [3]. Aissaoui et al. [10]. found that disease activity was the strongest predictor of fatigue in patients with AS. However, another study found that although disease activity has a strong influence on fatigue, the influence of psychological factors should also be considered [8].

Although patients with AS have severe fatigue symptoms, there is still controversy about the correlation factors that lead to fatigue in patients with AS. Therefore, the purpose of this study is to understand the fatigue status of patients with AS and analyze its possible correlation factors, so as to provide reference for taking appropriate measures in future clinical work to improve the fatigue status of AS patients, improve their daily life and work ability, promote patient rehabilitation, and thus improve patients' quality of life. This study was approved by the Medical Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

Clinical data

Diagnostic criteria

The diagnostic criteria for Western medicine adopted the revised AS New York standard proposed in 1984, and also referred to the classification criteria for axial spinal arthritis recommended by the International Association for the Evaluation of Spinal Arthritis (ASAS) in 2009.

Inclusion criteria

(1) Fulfilment of the diagnostic criteria for AS in Western medicine. (2) Age ≥ 16 years old. (3) Patients sign informed consent.

Exclusion criteria

(1) Serious lesions of the heart, liver, kidney and other vital organs, suffering from diseases of the blood and endocrine system. (2) Current history of active tuberculosis. (3) Patients with rheumatoid arthritis, psoriatic arthritis, inflammatory bowel disease and other rheumatological and immunological diseases. (4) Those who could not fully describe their condition completely and completed the questionnaire independently.

General information

A total of questionnaires were collected from all patients with AS who visited 12 hospitals in 9 centers in China between March 2022 and September 2023. Finally, 338 AS patients with complete data were included. Demographic

variables included age, sex, height, weight, BMI, etc. Clinical variables included course of disease, family history, extra-articular manifestations (including history of ophthalmia, intestinal infection and urinary tract infection), Functional Assessment of Chronic Illness Therapy Scale (FACIT-F) score, AS Disease Activity Score-C-reactive protein (ASDAS-CRP), AS disease activity score-erythrocyte sedimentation rate (ASDAS-ESR), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Function Index (BASFI), Bath Ankylosing Spondylitis Measurement Index (BASMI), Patient Global Assessment (PGA) score, night pain score, Depression Anxiety Stress Scale (DASS-21), AS International Community Health Index Assessment (ASAS-HI), human leukocyte antigen B27 (HLA-B27), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Method

Questionnaire

General information questionnaire

Investigating the patient's general information by using the general Information Questionnaire. The main contents of the survey included the patients' age, sex, height, weight, BMI, disease history, family history and other basic information, and the relevant data were collected through the questionnaire filled in by the patients themselves.

Functional Assessment of Chronic Illness Therapy Scale (FACIT-F) [11]

The patients' level of fatigue was assessed using the FACIT-F. The FACIT-F scale consisted of 13 items and assessed the impact of fatigue on the patient's daily life during the previous 7 days. A 0–4 scale was used, with 0 being not at all and 4 being very, the total score ranging from 0 to 52. The higher the score, the less fatigued the patient was.

AS Disease Activity Score (ASDAS) [12]

The patient's ASDAS-CRP and ASDAS-ESR were calculated. The ASDAS score could be divided into four stages: remission period (ASDAS < 1.3), period of low disease activity (1.3 ≤ ASDAS < 2.1), period of very high disease activity (2.1 ≤ ASDAS < 3.5) and period of very high disease activity (ASDAS ≥ 3.5).

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [12]

Disease activity was assessed using the BASDAI. It includes 6 questions about fatigue, spinal pain, joint pain or peripheral joint swelling, tenderness or sensitivity, severity, and duration of morning stiffness, each using a 10 cm VAS score, with a higher score indicating a higher disease activity index. Patients' disease activity can be divided into two stages based on the score: remission period (BASDAI < 4) and activity period (BASDAI ≥ 4).

Bath Ankylosing Spondylitis Function Index (BASFI) [12]

Functional status is determined by the BASFI. It includes 8 activities related to the patient's functional anatomy (bending, stretching, transferring, standing, turning around and climbing stairs) and 2 items that assess the patient's ability to perform activities of daily living. It is measured on a scale of 0–10, with higher scores indicating poorer function.

Bath Ankylosing Spondylitis Measurement Index (BASMI) [12]

The BASMI was used to assess axial range of motion in AS patients and objectively assess clinically significant changes in spinal motion. It consisted of 5 items that clinically measured cervical rotation, tragus-to-wall distance, lumbar flexion, lumbar lateral flexion, and intermalleolar distance.

Patient Global Assessment (PGA) score [13]

Evaluate the patient's global condition through the PGA. The PGA is scored on a scale of 0–3, and the PGA should include the middle logo of 1 and 2 (with a PGA word and charts of 0,1,2,3) without any additional assessment whether it is mild, moderate, etc. The relationship between PGA values and the severity of disease activity: (1) On the PGA scale, 0 means "no disease activity". (2) On the PGA scale, 3 means "the most severe disease activity". (3) 0.5 ≤ PGA ≤ 1, indicates mild disease activity. (4) 1< PGA ≤ 2 indicates moderate disease activity. (5) 2< PGA ≤ 3 indicates severe disease activity.

Night pain score [14]

The degree of the patient's pain at night was assessed using the VAS. The specific method of operation is relatively simple, by drawing a line on a piece of white paper, and the horizontal section of the line is the number 0, indicating that the patient has no pain; the other end of the line is the number 10, representing severe pain. The person is asked to record the level of pain by making a note on this horizontal line according to how they feel the pain. The VAS pain scale indicates the level of pain as follows: (1) 0 indicates that the patient feels no pain. (2) a score below 3 indicates that the patient has mild but tolerable pain. (3) 4–6 points: patients have obvious pain, affecting sleep quality, is still tolerable. (4) 7–10 points: patients have severe and unbearable pain, affecting sleep quality and appetite.

Depression-Anxiety-Stress Scale (DASS-21) [15]

The level of anxiety, depression and stress was assessed using the DASS-21. The scale contains 21 items, and the depression, anxiety and stress subscales each contain 7 items, all of which are scored on 4-point scale ranging from 0 (inconsistent) to 3 (always consistent). The score of each subscale is multiplied by 2, subscale score.

The higher the score value, the worse mood is. On the depression subscale, 10, 14 and 21 are the cut-off values for mild, moderate and severe depression respectively; on the anxiety subscale, 8, 10 and 15 are the cut-off values for mild, moderate and severe anxiety respectively; on the stress subscale, 15, 19 and 26 are the cut-off values for mild, moderate and severe stress respectively.

AS International Community Health Index (ASAS-HI) Assessment [16]

The health status of patients with AS was assessed using the ASAS-HI. The ASAS-HI is a linear comprehensive measurement scale consisting of 17 items with the option of responding "I agree" (0 points) or "I disagree" (1 points). The total ASAS-HI score ranges from 0 to 17 points, with higher scores indicating poorer health for the patient.

Laboratory indicator

Human leukocyte antigen B27 (HLA-B27), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured in venous blood from patients at enrolment.

Study method

Relevant questionnaires and observational indicators were collected for AS patients at their first visit. All the rheumatologists involved in the case collection were trained by the research group. Patient survey information was collected by uniformly trained rheumatologists and questionnaires were completed according to standard practice.

Statistical method

SPSS 27.0 statistical software was used for data analysis. The current fatigue status of AS patients was determined by basic statistical analysis of the collected questionnaire data. The current fatigue status of AS patients was obtained. In order to evaluate the severity of fatigue in AS patients, their scores were divided into four grades: no or very mild fatigue ($40 \le$ FACIT-F ≤ 52), mild fatigue ($27 \le$ FACIT-F ≤ 39), moderate fatigue ($14 \le$ FACIT-F ≤ 26) and severe fatigue ($0 \le$ FACIT-F ≤ 13) [11]. Spearman correlation analysis was used to analyze the correlation between statistical variables and fatigue in AS patients, and we considered that the significance level of "$P < 0.05$" was statistically significant. Multiple linear regression analysis was performed to determine the predictors of fatigue in AS patients by combining the fatigue status of AS patients with the statistically significant influencing factors obtained from Spearman correlation analysis, and the significance level of "$P < 0.05$" was considered to be statistically significant.

Result

Analysis of fatigue status in 338 patients with AS

FACIT-F score

Statistical analysis of the FACIT-F scores showed that fatigue was evident in 37.9% of 338 patients with AS. Among them, there were 210 cases (62.1%) with no or very mild fatigue ($40 \le$ FACIT-F ≤ 52), 106 cases (31.4%) with mild fatigue ($27 \le$ FACIT-F ≤ 39), 22 cases (6.5%) with moderate fatigue ($14 \le$ FACIT-F ≤ 26), and 0 cases (0) with severe fatigue ($0 \le$ FACIT-F ≤ 13).

General clinical data

The general clinical data of AS patients were statistically analyzed. The results showed that among the 338 AS patients, 270 were males (79.9%) and 68 were females (20.1%). Age 17–71 years, mean (38.61 ± 11.05) years, height 100–191 cm, mean (165.19 ± 0.74) cm; weight 37.5–120 kg, mean (66.90 ± 0.74) kg, body mass index (BMI) 16–58, mean (24.68 ± 0.28), disease course ranged from 1 month to 43 years, mean (11.36 ± 0.46) years. There were 80 cases (76.3%) with family history and 258 cases (23.7%) without family history, 83 cases (24.6%) had extra-articular manifestations and 255 cases (75.4%) had no extra-articular manifestations, 202 cases (59.8%) were HLA-B27 positive and 136 cases (40.2%) were negative. 70 cases (20.7%) in remission period (ASDAS-CRP < 1.3), 109 cases (32.2%) in period of low disease activity ($1.3 \le$ ASDAS-CRP < 2.1), 125 cases (37.0%) in period of high disease activity ($2.1 \le$ ASDAS-CRP < 3.5) and 34 patients (10.1%) in period of very high disease activity (ASDAS-CRP ≥ 3.5). 91 patients (26.9%) were in remission period (ASDAS-ESR < 1.3), 84 patients (24.9%) were in period of low disease activity ($1.3 \le$ ASDAS-ESR < 2.1), 133 patients (39.3%) were in period of high disease activity ($2.1 \le$ ASDAS-ESR < 3.5) and 30 cases (8.9%) were in period of very high disease activity (ASDAS-ESR ≥ 3.5). 264 cases (78.1%) were in remission period (BASDAI < 4) and 74 cases (21.9%) were in active period (BASDAI ≥ 4).

Analysis of factors influencing fatigue in 338 patients with AS

Spearman correlation analysis

The Spearman correlation analysis of fatigue in AS patients with different statistical variables showed that age, disease course, extra-articular manifestation, ASDAS-CRP, ASDAS-ESR, BASDAI, PGA, BASFI, BASMI, night pain, ASAS-HI, anxiety, depression and stress were the main factors influencing fatigue in patients ($P < 0.05$), as shown in Table 1.

Multiple linear regression analysis

Statistically significant influencing factors obtained by Spearman correlation analysis ($P < 0.05$): Multiple linear regression analysis was performed on age, disease course,

Table 1 Analysis of Spearman correlation coefficients between fatigue and statistical variables in AS patients (*N* = 338)

Items	Correlation coefficient(*r*)	Significance(*P*)	95% Confidence interval(95%CI)
Sex	0.080	0.167	-0.037, 0.195
Age	-0.213	< 0.001	-0.316, -0.106
Height (cm)	0.069	0.203	-0.041, 0.178
Weight (kg)	0.007	0.898	-0.103, 0.117
BMI	-0.103	0.059	-0.210, 0.007
Disease course	-0.231	< 0.001	-0.333, -0.125
Family history	-0.053	0.330	-0.162, 0.057
Extra-articular manifestation	-0.121	0.026	-0.228, -0.012
HLA-B27	0.003	0.953	-0.107, 0.113
ASDAS-CRP	-0.464	< 0.001	-0.546, -0.373
ASDAS-ESR	-0.441	< 0.001	-0.525, -0.348
BASDAI	-0.508	< 0.001	-0.585, -0.422
PGA	-0.498	< 0.001	-0.576, -0.411
BASFI	-0.512	< 0.001	-0.589, -0.427
BASMI	-0.304	< 0.001	-0.406, -0.194
Night pain	-0.426	< 0.001	-0.512, -0.331
ASAS-HI	-0.623	< 0.001	-0.686, -0.551
Depression	-0.611	< 0.001	-0.676, -0.537
Anxiety	-0.550	< 0.001	-0.622, -0.468
Stress	-0.570	< 0.001	-0.640, -0.491

extra-articular manifestation, ASDAS-CRP, ASDAS-ESR, BASDAI, PGA, BASFI, BASMI, night pain, ASAS-HI, anxiety, depression and stress. The results showed that, the model fit was good (R square = 0.666), and the autocorrelation of independent variables was not significant (D-W = 1.369). Extra-articular manifestation BASDAI, night pain, ASAS-HI and depression were independent predictors of fatigue in patients ($P < 0.05$), as shown in Table 2.

Analysis of factors influencing fatigue in AS patients with different degrees of fatigue

Factors influencing fatigue in patients with AS in the no or very little fatigue group

Spearman correlation analysis The results of Spearman correlation analysis of fatigue and various statistical variables in 210 patients with no or very little fatigue showed that age, ASDAS-CRP, ASDAS-ESR, BASDAI, BASFI, ASAS-HI, depression and anxiety were the main influencing factors of fatigue ($P < 0.05$), as shown in Table 3.

Multiple linear regression analysis Statistically significant influencing factors obtained by Spearman correlation analysis ($P < 0.05$): Multiple linear regression analysis was performed on age, ASDAS-CRP, ASDAS-ESR, BASDAI, BASFI, ASAS-HI, depression and anxiety, and the results showed that age, BASDAI and ASAS-HI was an independent predictor of fatigue ($P < 0.05$), as shown in Table 4.

Factors influencing fatigue in patients with AS in the mild and moderate fatigue group

Spearman correlation analysis The Spearman correlation analysis of fatigue and statistical variables in 128 patients with mild and moderate fatigue showed that ASDAS-CRP, BASDAI, PGA, BASFI, night pain, ASAS-HI, depression, anxiety and stress were the main factors influencing patients' fatigue ($P < 0.05$), as shown in Table 5.

Multiple linear regression analysis The statistically significant influencing factors obtained by Spearman correlation analysis ($P < 0.05$), height, BMI, disease course, BASFI, BASMI, night pain, ASDAS-CRP, ASDAS- ESR, BASDAI, PGA, ASAS-HI, depression, anxiety and stress

Table 2 Multiple linear regression analysis of fatigue in patients with AS (*N* = 338)

Items	Unnormalized Coefficient		Standardized Coefficient			
	B	Standard error	Beta	t	Significance(P)	95% Confidence interval(95%CI)
Age	-0.049	0.026	-0.075	-1.880	0.061	-0.100,0.002
Disease course	0.012	0.041	0.015	0.297	0.767	-0.069,0.094
Extra-articular manifestation	-1.295	0.594	-0.078	-2.178	0.030	-2.465,-0.124
BASFI	-0.103	0.143	-0.036	-0.724	0.470	-0.384,0.178
BASMI	-0.054	0.121	-0.024	-0.445	0.656	-0.292,0.184
Night pain	-0.323	0.135	-0.113	-2.397	0.017	-0.588,-0.058
ASDAS-CRP	-0.316	0.529	-0.045	-0.599	0.550	-1.357,0.724
ASDAS-ESR	0.841	0.436	0.122	1.930	0.055	-0.017,1.698
BASDAI	-0.950	0.210	-0.258	-4.532	< 0.001	-1.362,-0.537
PGA	-0.126	0.160	-0.047	-0.789	0.431	-0.442,0.189
ASAS-HI	-0.247	0.063	-0.182	-3.920	< 0.001	-0.371,-0.123
Depression	-0.472	0.089	-0.369	-5.304	< 0.001	-0.647,-0.297
Anxiety	0.041	0.108	0.026	0.375	0.708	-0.172,0.253
Stress	-0.152	0.083	-0.129	-1.827	0.069	-0.315,0.012

Table 3 Analysis of Spearman correlation coefficient between fatigue and statistical variables in AS patients with no or very little fatigue group ($N=210$)

Items	Correlation coefficient(*r*)	Significance(*P*)	95% Confidence interval(95%CI)
Sex	-0.019	0.793	-0.165, 0.128
Age	-0.176	0.011	-0.307, -0.037
Height (cm)	0.077	0.267	-0.063, 0.214
Weight (kg)	0.025	0.723	-0.115, 0.163
BMI	-0.082	0.237	-0.219, 0.058
Disease course	-0.131	0.057	-0.266, 0.008
Family history	-0.071	0.308	-0.208, 0.069
Extra-articular manifestation	0.008	0.904	-0.131, 0.148
HLA-B27	0.054	0.439	-0.086, 0.192
ASDAS-CRP	-0.175	0.011	-0.306, -0.036
ASDAS-ESR	-0.154	0.025	-0.288, -0.015
BASDAI	-0.288	< 0.001	-0.411,-0.155
PGA	-0.123	0.075	-0.258,0.017
BASFI	-0.257	< 0.001	-0.383,-0.122
BASMI	-0.104	0.154	-0.247,0.043
Night pain	-0.072	0.299	-0.210,0.068
ASAS-HI	-0.354	< 0.001	-0.470,-0.226
Depression	-0.216	0.002	-0.345,-0.079
Anxiety	-0.219	0.001	-0.348,-0.083
Stress	-0.135	0.050	-0.270,0.004

Table 5 Analysis of Spearman correlation coefficient between fatigue and statistical variables in patients with AS in the mild and moderate fatigue group ($N=128$)

Items	Correlation coefficient(*r*)	Significance(*P*)	95% Confidence interval(95%CI)
Sex	0.048	0.621	-0.146, 0.238
Age	-0.079	0.375	-0.254, 0.101
Height (cm)	-0.115	0.196	-0.288, 0.065
Weight (kg)	-0.123	0.167	-0.295, 0.057
BMI	-0.078	0.381	-0.253, 0.102
Disease course	0.092	0.303	-0.088, 0.266
Family history	-0.041	0.649	-0.218, 0.139
Extra-articular manifestation	-0.064	0.476	-0.239, 0.116
HLA-B27	0.137	0.123	-0.043, 0.308
ASDAS-CRP	-0.176	0.047	-0.343, 0.003
ASDAS-ESR	-0.137	0.122	-0.308, 0.042
BASDAI	-0.309	< 0.001	-0.462, -0.138
PGA	-0.262	0.003	-0.421, -0.087
BASFI	-0.229	0.009	-0.392, -0.053
BASMI	0.009	0.922	-0.184, 0.202
Night pain	-0.264	0.003	-0.422, -0.089
ASAS-HI	-0.282	0.001	-0.439, -0.109
Depression	-0.466	< 0.001	-0.595, -0.314
Anxiety	-0.488	< 0.001	-0.613, -0.339
Stress	-0.515	< 0.001	-0.635, -0.371

were analyzed by multiple linear regression analysis. The results showed that BASMI, PGA and anxiety were independent predictors of fatigue ($P<0.05$), as shown in Table 6.

Discussion

AS is a chronic inflammatory disease, can lead to patients with low back pain at night, morning stiffness, fatigue and limb joint swelling pain, some patients may also appear skin, eyes, intestinal diseases and other discomfort, chronic progression will appear bone structure destruction and reconstruction, and then lead to patients with irreversible damage to life and social functions. Fatigue as a subjective feeling of discomfort, often plagues people with AS, and can seriously affect their life and work. Fatigue is closely related to the other symptoms of AS (stiffness and pain, etc.) and is negatively affected by sleep disturbance, often resulting in a severely reduced quality of life and ability to work in these patients [2]. Long-term chronic fatigue can have serious negative consequences for patients, such as negative emotions, sleep deprivation, self-neglect, impaired immune system function, resulting in a reduced ability to cope, which in turn affects their recovery from the disease [7].

The results of a prospective cohort study from Northern Finland suggest that height is associated with the incidence of knee Osteoarthritis (OA) [17]. The study of middle-aged British women by Chingford et al. also

Table 4 Multiple linear regression analysis of fatigue in patients with AS in the no or very little fatigue group ($N=210$)

Items	Unnormalized coefficient		Standardized coefficient			
	B	Standard error	Beta	t	Significance(P)	95% Confidence interval(95%CI)
Age	-0.042	0.016	-0.173	-2.661	0.008	-0.073, -0.011
ASDAS-CRP	-0.101	0.324	-0.033	-0.312	0.755	-0.739, 0.537
ASDAS-ESR	0.224	0.285	0.077	0.787	0.432	-0.337, 0.785
BASDAI	-0.331	0.140	-0.193	-2.356	0.019	-0.607, -0.054
BASFI	-0.045	0.104	-0.030	-0.431	0.667	-0.249, 0.160
ASAS-HI	-0.152	0.040	-0.254	-3.779	< 0.001	-0.231, -0.073
Depression	-0.070	0.084	-0.070	-0.840	0.402	-0.236, 0.095
Anxiety	-0.074	0.078	-0.080	-0.939	0.349	-0.228, 0.081

Table 6 Multiple linear regression analysis of fatigue in patients with AS in the mild and moderate fatigue group ($N=128$)

Items	Unnormalized coefficient		Standardized coefficient			
	B	Standard error	Beta	t	Significance(P)	95% Confidence interval(95%CI)
ASDAS-CRP	0.585	0.659	0.093	0.887	0.377	-0.721, 1.890
BASDAI	-1.122	0.300	-0.379	-3.739	< 0.001	-1.717, -0.528
PGA	-0.301	0.222	-0.119	-1.354	0.178	-0.741, 0.139
BASFI	0.020	0.178	0.009	0.110	0.913	-0.333, 0.372
Night pain	0.022	0.179	0.011	0.122	0.903	-0.333, 0.376
ASAS HI	-0.008	0.118	-0.006	-0.069	0.945	-0.241, 0.225
Depression	-0.285	0.109	-0.331	-2.618	0.010	-0.501, -0.069
Anxiety	-0.030	0.131	-0.026	-0.229	0.819	-0.288, 0.229
Stress	-0.218	0.106	-0.245	-2.061	0.042	-0.427, -0.008

found that taller women had a higher risk of developing knee OA [18]. However, our results did not find a clear correlation between height and fatigue, which may have something to do with people we studied. We believe that the taller the AS patients, the more fatigued they were the possible reason is that patients with a taller stature often need a longer stride length and more muscle movement to support the body when walking, and at the same time due to the body structure, the spinal joint bears more impact and load, which is easy to lead to fatigue. A study of fatigue status in patients with rheumatoid arthritis (RA) showed that obesity was an independent predictor of fatigue [19]. One intervention for RA patients was to reduce the amount of time spent sitting on a daily basis, and it was found that there was a tendency for the Waist-to-Hip Ratio (WHR) to decrease in RA patients, and that patients experienced some relief from fatigue [20]. Eder et al. [21] confirmed that obesity is associated with delayed onset psoriasis and psoriatic arthritis (PsA). The higher the BMI of people with AS, the more likely they are to feel tired. The possible reason for this is that excess fat increases the exercise the physical strain on patients, resulting in impaired cardiovascular function, metabolic disorders and breathing difficulties. But our study found no significant correlation between BMI and fatigue in patients with AS. Previous reports have shown that patients with AS who adhere to standard exercise regimens have reduced disease activity and improved quality of life, suggesting that patients with AS should be encouraged to adhere to moderate exercise to maintain a healthy weight [22]. In addition, the longer the disease course in patients with AS, the more severe the adverse effects on physiological and psychological functions, easily leading to organ dysfunction, neuromuscular conduction disorders and muscular dystrophy and other hazards, followed by fatigue, muscle pain and other symptoms [7]. This is consistent with our findings that there is a correlation between disease duration and fatigue. Law et al. [23]. pointed out that the ESR and VAS scores for overall fatigue were significantly higher in women with AS than those in men. However, there was no significant association between sex and fatigue in our study, which may be due to differences in the population included, with only 68 women (20.1%) in our study.

Disease activity is an important assessment index that reflects the disease status at the time point of the patient, which may reflect the inflammatory activity of the disease, and is often used in clinical monitoring of the change of the patient's condition change and treatment effect. Currently, the commonly used indicators to assess disease activity in AS include ASDAS-CRP, ASDAS-ESR and BASDAI, etc. Previous studies have shown a correlation between disease activity and fatigue in patients with AS [4, 12]. Alkan et al. [24] evaluated 110 patients with AS and 40 healthy controls using the Multidimensional Fatigue Assessment (MAF) and showed that MAF scores were significantly associated with BASDAI in all patients. A cohort study also confirmed BASDAI as an independent predictor of fatigue severity in patients with AS [9]. Consistent with the results of previous studies, we also found that disease activity (ASDAS-CRP, ASDAS-ESR, BASDAI, and PGA) was significantly correlated with fatigue in AS patients ($P<0.05$), and the greater the severity of fatigue, the more significant the effect of disease activity on fatigue. Studies have shown that the higher the disease activity of patients with AS, the greater the decline in various functions of the patient's body and the impairment of organ function. When patients are in a state of high disease activity, there are risks such as organ dysfunction, nervous system disorders and immune system imbalance, which will lead to an increase in patients' fatigue levels [10]. In addition, patients with high disease activity often have more obvious clinical symptoms, such as joint mobility, stiffness, poor joint motion, etc., which cause physiological and psychological discomfort to patients, and create conditions for fatigue.

Studies have shown that the quality of life of patients with AS is significantly lower than that of healthy controls. Schneeberger et al. [25] showed that fatigue affects the quality of life in patients with AS. The measurement

health-related quality of life (HR-QoL) is considered an important component of a comprehensive assessment of the health status of patients with AS [12]. As a result of a multi-center international study conducted in 23 countries, the ASAS-HI can be used to assess the overall impact of spinal arthritis on the health of patients (with a focus on the early stages of disease) [16]. This study also found that fatigue was significantly associated with the ASAS-HI, possibly because he relationship between fatigue symptoms and disease activity is further reflected in health status, or because health status itself contributes to fatigue. A cross-sectional study of 385 patients with AS highlighted pain as the main factor associated with fatigue [26]. Our results also showed that there was a strong correlation between night pain and the level of fatigue experienced by patients. As a common symptom of AS patients, nocturnal not only brings the subjective feeling of discomfort to patients, but also seriously affects the quality of the patients' quality of life and work, and brings the dual negative effects of physiology and psychology to the patients, thus exacerbating the degree of fatigue.

It has been reported that fatigued patients have more overt anxiety, poorer physical function and lower quality of life compared to non-fatigued patients [27]. We also found that AS patients with fatigued had greater functional disability and anxiety compared with patients with non-fatigued AS, all of which contributed to a reduction in patients' quality of life [2]. Consistent with the results of previous studies, we also found that psychological factors such as anxiety, depression and stress had a significant impact on fatigue in AS patients, and the greater the degree of fatigue, the more pronounced the impact of psychological factors on fatigue. Modern research shows that bad mood (anxiety, depression, stress) can lead to patients with autonomic nervous dysfunction, endocrine disorders and other hazards, seriously affecting the patient's physical and mental health of patients, resulting in increased fatigue [3, 5].The study found that AS activity triggered fatigue by inducing psychological changes, and head MRI imaging found that the left thalamic volume of severely fatigued AS patients was significantly larger than that of non-fatigued AS patients and healthy controls, suggesting the role of neuropsychology in AS-related fatigue [3].

Conclusion

In this article we have confirmed the patients' fatigue levels were closely related to disease activity (ASDAS, BASDAI and PGA) and psychological factors (anxiety, depression and stress). At the same time, the influence of disease activity and psychological factors on fatigue was more pronounced the higher the level of fatigue. As one of the common concomitant symptoms of AS patients, fatigue will be worsened with the worsening of disease, not only that, fatigue will also affect the physical and mental health of patients to a certain extent, and further aggravate the disease. Modern clinical practice places more and more emphasis on the "bio-psycho-social" medical model, looking at the patient as a whole person, rather than just treating the disease itself [28]. Fatigue as one of the major symptoms of patients, seriously affect the patient's prognosis and quality of life, clinical work should pay attention to AS patients' fatigue, in order to maximize the patient's physical and mental discomfort, reduce the poor prognosis of the disease and improve the quality of life of patients.

The limitations of this study are mainly reflected in the sample and research methods. First, the sample size of this study was relatively small. The limited sample size may not fully represent the target population, limiting the generalizability of the results. The smaller sample may miss some special cases or group characteristics, which may have a certain impact on the accuracy and stability of the conclusions. Secondly, in terms of study design, this study adopted a cross-sectional study design, which can only observe and analyze the relationship between variables at a specific time point and cannot determine causality. Finally, this study has not yet evaluated the effectiveness of drug treatment for fatigue in AS patients, and we expect that relevant experimental verification can be carried out in the future.

Abbreviations

AS	Ankylosing spondylitis
FACIT-F	Functional Fatigue Scale in Chronic Illness Therapy-F score
ASDAS	AS disease activity score
BASDAI	Bath ankylosing spondylitis disease activity index
BASFI	Bath ankylosing spondylitis Functional index
BASMI	Bath ankylosing spondylitis Measurement index
PGA	Physical assessment score
VAS	Visual analogue scale
DASS-21	Depression anxiety Stress scale
ASAS HI	AS International Social Health Index
ASAS	The International Association for the Evaluation of Spinal Arthritis
BMI	Body Mass Index
HLA-B27	Human leukocyte antigen B27 level
CRP	C-reactive protein level
ESR	Erythrocyte sedimentation rate level
OA	Osteoarthritis
RA	Rheumatoid arthritis
PsA	Psoriatic arthritis
WHR	Waist-to-Hip Ratio
MAF	Multidimensional Fatigue Assessment
HR-QoL	The measurement health-related quality of life

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Author contributions

S and Y have contributed equally to this work. S and Y were responsible for data analysis and article writing. G, Q, Y and C contributed to study conception and design. All authors were responsible for the acquisition of data. This paper has been revised by L. All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval in accordance with the Declaration of Helsinki was obtained from the Medical Ethics Committee of Guang'anmen Hospital (Approval number: 2022–108–KY). The informed consent to participate was obtained from all of the participants in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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