Effects of ankylosing spondylitis and non-radiographic axial spondyloarthropathy on female sexual functions

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Abstract

Objective

Rheumatologic diseases may impair the quality of life (QoL) by affecting sexual functions in different ways. We aimed to evaluate sexual functions and the disease-related variables, physical and psychogenic states in female patients with ankylosing spondylitis and non-radiographic axial spondyloarthropathy.

Methods

A total of 98 women with axial spondyloarthropathy (axSpA) and 99 healthy females were included in the study. The axSpA group was divided into two subgroups as ankylosing spondylitis (AS) and non-radiographic axial spondyloarthropathy (nr-axSpA) (62 AS and 36 nr-axSpA). The patients' disease-related variables recorded. All the women in the axSpA and control groups were evaluated gynaecologically. The female sexual function index (FSFI), Health Status Questionnaire [Short Form (SF)-36], and Hospital Depression and Anxiety Scale (HADS) were applied to all participants.

Results

Clitoral and labial atrophy and speculum pain score were significantly higher in the axSpA group ($p<0.05$). The FSFI and QoL-SF-36 scores were significantly lower and the HAD-D and HAD-A scores were significantly higher of in the axSpA group than in the control group ($p<0.05$ for all). There was no significant between the axSpA subgroups in terms of the FSFI, QoL-SF-36 and HAD scores.

Conclusion

In elderly women with axSpA, disease duration and limitation of movement are more effective in genital atrophy and sexual functions, but there is no difference between those with AS and nr-axSpA in relation to sexual functions and psychological burden.

Key words

ankylosing spondylitis, non-radiographic axial spondyloarthropathy, female sexual functions, disease activity, genital atrophy

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Introduction

Axial spondyloarthropathies (axSpA) refers to a multisystem disease characterised by the inflammation of the vertebra, peripheral joint and surrounding structures. The concept of axSpA covers cases without definitive radiographic sacroiliitis on x-ray examination (nr-axSpA) and those with radiographic sacroiliitis according to the modified New York criteria (AS). AS is the prototype of axSpA-group diseases. It is a systemic, chronic and inflammatory rheumatic disease with extra articular clinical findings, and its aetiology is unknown (1).

The period in which there is inflammatory backache but no sacroiliitis is detected radiographically is called nr-axSpA. Although there are some studies stating that nr-axSpA disease is the early form of AS and that the disease burden is similar in nr-axSpA and AS (2-4), it is argued that both diseases are different from each other (5). When these diseases are examined genetically, HLA-B27 ratios are lower in nr-axSpA, and when evaluated demographically, the rate of men in AS patients supports this difference (6). This argument is further supported by the difference between the two diseases in relation to their response rates to biological therapy (7).

Sexual function is an important part of human life and is associated with quality of life (QoL). Rheumatic diseases often affect the musculoskeletal system, but can also cause internal organ involvement; therefore, they result in different degrees of dysfunction and affect all life activities, including social, economic, psychological and sexual functions (8).

Sexual dysfunction may occur in different forms and at varying degrees depending on the characteristic of prevailing symptoms in many rheumatologic diseases (9). The causes of sexual dysfunction in such diseases depend on many factors: *e.g.* pain, weakness, fatigue, stiffness, functional insufficiency, depression, anxiety, negative body image, decreased libido, hormonal insufficiency, and drug use (10-12). The effect of AxSpA on sexual function is overlooked and even neglected in daily practice for both patients and healthcare professionals. The aim of this study was to evaluate the variables that determine the course and burden of axSpA and investigate the physical and psychogenic states and sexual functions in female patients with AS and nr-axSpA.

Material and methods

The study was designed as a single-centre cross-sectional case control study. A total of 98 women with axSpA (62 with AS and 36 with nr-axSpA) who presented to the rheumatology outpatient clinic at Atatürk Training and Research Hospital between May 2015 and July 2019 were included in the axSpA group, and 99 otherwise healthy females who presented to the gynecology outpatient clinic for reasons other than sexual dysfunction were included in the control group. The diagnosis of the patients in the axSpA group was made according to the Assessment of Spondylo Arthritis International Society 2009 New York criteria (13), and the methods and drugs used for the treatment of the patients were recorded. The patients' age, gravidity, parity, body mass index (BMI), educational status, smoking status, menarche age, menopause status and duration, age at which axSpA was diagnosed and disease duration, serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and human leukocyte antigen B27 (HLA-B27) positivity were recorded. Disease-related variables (activity and function data, etc.), Bath AS Metrology Index (BASMI), Bath AS Functional Index (BASFI), Bath AS Disease Activity Index (BASDAI), enthesitis scores, Health Assessment Questionnaire (HAQ) and Visual Analog Scale-Pain (VAS-Pain) scores were evaluated and recorded by the same rheumatologist. All patients in the axSpA and control groups were evaluated by the same gynecologist, and both researchers had at least 15 years of clinical experience.

Women under 18 and over 65 years were excluded from the study. Furthermore, those with communication disorders, pregnancy, a history of hysterectomy or vaginal surgery, cardiovascu-

lar, pulmonary, hepatic, renal, haematologic and gynaecologic oncological diseases, and endocrine disorders such as diabetes mellitus and thyroid dysfunction, psychiatric disorders, those using antihypertensive, antidepressant, anxiolytic, antipsychotic and antiepileptic agents, and those using oral or vaginal oestrogen were also excluded. The Female Sexual Function Index (FSFI), Health Status Questionnaire [Short Form (SF)-36], and Hospital Depression and Anxiety Scale (HADS) were applied to the women in both groups, and their scores were determined. The data obtained from the axSpA and control groups were compared. The patients in the axSpA group were further divided into the subgroups of AS and nr-axSpA, and statistical comparisons were also undertaken between these subgroups. A multivariate linear regression analysis was performed, and the correlation of sexual function with other parameters was examined. The study was approved by the institutional Ethical Committee (no: 2015/84), and written informed consent was obtained from all patients participating in the study.

Determination of sexual function (FSFI)

The sexual functions of women participating in the study were evaluated using the validated Turkish version of FSFI developed by Rosen *et al*. (14-15). This index includes participants' evaluations of sexual desire, arousal, lubrication, orgasm, satisfaction, pain, and total sexual intercourse. Scoring between 0–5 or 1–5 is made for each domain. The total score ranges from 2 to 36, and higher scores indicate better function.

The SF-36 questionnaire

QoL was measured using the Turkish version of the SF-36 questionnaire consisting of the following eight domains: physical functioning (PF), physical role challenge (PR), emotional role difficulty (ER), energy/vitality (VT), mental health (MH), social functionality (SF), bodily pain (BP), and general perception of health (GH) (16-17). The items in all eight domains are scored between 0 and 100, with 0 referring to the worst and 100 referring to the best health indicator. The items in the questionnaire reflect the health status of the patients over the last four weeks.

Table I. Demographic and clinical characteristics of the study groups.

	axSpA group (n=98)	Control group (n=99)	*p*
Age (years)	48 (28-65)	47 (27-64)	0.975
Gravida	3 (0-11)	3 (0-6)	0.493
Parity	2 (0-8)	2 (0-8)	0.539
Previous births			
C/S	64 (65.3%)	68 (68.7%)	0.511
VD	34 (34.7%)	31 (31.3%)	
BMI (kg/m^2)	25.2 ± 3.1	24.6 ± 2.8	0.293
Smoking			
Yes	76 (77.6%)	76 (76.8%)	0.810
No	22 (22.4%)	23 (23.2%)	
Education			
<10 years	60 (61.2%)	59 (59.6%)	0.251
>10 years	38 (38.8%)	40 (40.4%)	
Age of menarche (years)	13 (10-18)	13 (11-17)	0.155
Menopause			
Yes	15 (15.3%)	16 (16.2%)	0.863
No	83 (84.7%)	83 (83.8%)	
Duration of menopause (years)	5.1 (01.-20)	4.9 (0.1-22)	0.152
Clitoral atrophy			
Yes	24 (24.7%)	10 (10.3%)	**0.003**
No	74 (75.3%)	89 (89.7%)	
Labial atrophy			
Yes	22 (22.6%)	9 (9.1%)	**<0.001**
No	76 (77.4%)	90 (90.9%)	
Vaginal atrophy			
Yes	20 (20.6%)	16 (16.2%)	0.421
No	78 (79.4%)	83 (83.8%	
Feeling of dryness in vagina			
Yes	30 (30.6%)	41 (41.4%)	0.099
No	68 (69.4%)	58 (58.6%)	
Cervical atrophy			
Yes	15 (15.3%)	13 (13.1%)	0.735
No	83 (84.7%)	86 (86.9%)	
Speculum pain score	4 (0-10)	3 (0-10)	**<0.001**
Vaginal infection			
Yes	22 (22.4%)	23 (23.2%)	0.809
No	76 (77.6%)	76 (76.8%)	
Atrophy in smear			
Yes	23 (23.5%)	16 (16.2%)	0.173
No	75 (76.5%)	83 (83.8%)	

axSpA: axial spondyloarthropathy; C/S: Cesarean section; VD: vaginal delivery; BMI: body mass index. Values given as median (min-max).

HADS

This scale was developed by Zigmond and Snaith (18) to determine patients' anxiety and depression levels, as well as changes in severity. It consists of a total of 14 items, seven on depression and seven on anxiety. The cut-off points for the depression and anxiety subscales were determined as 7 and 10, respectively. In the current study, the Turkish version of HADS was used (19).

Other questionnaires

BASDAI, BASFI, VAS-pain, and HAQ were also completed by the participants. BASDAI was performed to determine the disease activity of the patients within the last week and BASFI to determine their functional limitations. Higher scores are associated with higher disease activity and worse physical functions (20). VAS-pain was used to assess the overall pain status over the past week based on a scale of 0 to 100, with 0 indicating no pain and 100 representing extreme pain. HAQ consists of 20 items that measure the physical activities of patients in daily life. The HAQ score is calculated as a minimum of 0 and a maximum of 3. A

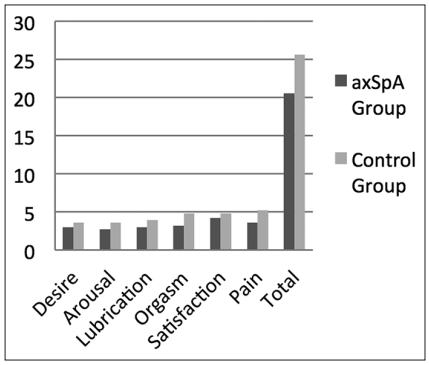

Fig. 1. FSFI scores of the study groups (p<0.001).
FSFI: Female Sexual Function Index; axSpA: axial spondyloarthropathy.

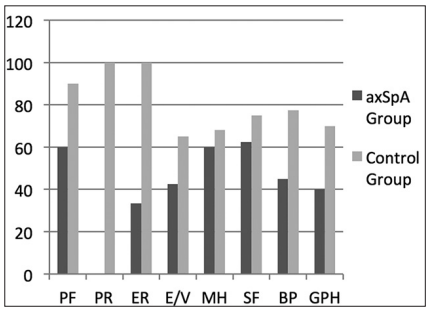

Fig. 2. SF-36 quality of life scores of the study groups (p<0.001).
SF-36: Short Form-36; axSpA: axial spondyloarthropathy; PF: physical functioning; PR: physical role challenge; ER: emotional role difficulty; E/V: energy/vitality; MH: mental health; SF: social functionality; BP: bodily pain; GPH: general perception of health.

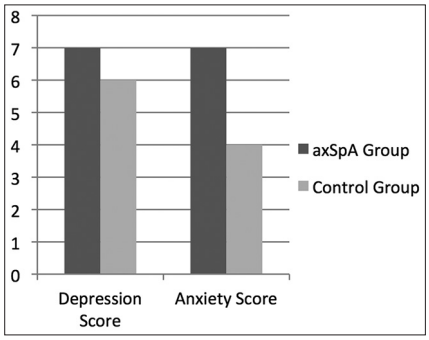

Fig. 3. HADS scores of the study groups (p<0.05).
HADS: Hospital Depression/Anxiety Scale; axSpA: axial spondyloarthropathy.

higher score indicates a lower health status. If the HAQ score is above 2, it is recommended to form a bone and muscle scan on the patient (21).

Laboratory variables and examinations

Serum samples were taken from all the patients in the axSpA group, and their CRP and ESR values were measured. The HLA b27 status of the patients in the axSpA group was recorded. The patients' mobility was measured using BASMI. A higher BASMI score indicates less spinal mobility (22).

All the participants underwent a gynaecological examination in the lithotomy position. The loss of rugae in the vagina, shrinkage and thinning of the mucosa, and introitus stenosis were evaluated in favor of vaginal atrophy, reduction of subcutaneous fat in the labia majora was evaluated as labial atrophy, and reduction in size and even retraction of the clitoral prepuce was interpreted as clitoral atrophy. Pain sensation on speculum examination was assessed by VAS (rated from 0 to 10) (23). Vaginal culture and cervicovaginal smear were analysed, and the findings were recorded.

Statistics

Statistical analysis was performed using SPSS for Windows, version 23.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation (SD) or median (minimum-maximum) values and as numbers or percentages where appropriate. The distribution of

Table II. Demographic data, disease-related variables, drug uses, FSFI, SF-36 quality of life scores and HADS scores of the axSpA subgroups.

	Ankylosing spondylitis (n=62)	Non-radiographic axSpA (n=36)	p
Age (years)	48 (28-65)	39 (28-56)	**<0.001**
Age of diagnosis (years)	43 (25-65)	38 (25-53)	**<0.001**
Duration of disease (years)	5 (1-30)	2 (1-6)	**0.001**
CRP (mg/l)	12.15 (3.4-269)	5.6 (3.4-22.7)	**<0.001**
ESR (mm/h)	20 (5-61)	20 (7-43)	0.255
Enthesitis score	2 (1-5)	2 (0-4)	0.083
Pain ^{VAS} (cm)	50 (20-80)	50 (30-80)	0.119
HAQ	0.3 (0-0.8)	0.2 (0.1-0.7)	0.084
HLA B27 positivity (n -%)	44 (71%)	14 (40%)	**0.003**
BASDAI	5.3 (1.2-6.8)	5.1 (1-8)	0.277
BASMI	1 (0-5)	0.2 (0-2)	**<0.001**
BASFI	10 (0.4-10)	1.4 (0-3.2)	**<0.001**
Fatigue score	60 (30-80)	60 (30-80)	0.852
Drug use			
Anti-TNF	9 (14.5%)	4 (11.1%)	**0.029**
Salazopyrin	32 (51.6%)	10 (27.8%)	
Other	21 (33.9%)	22 (61.1%)	
FSFI score			
Desire	3.0 (1.2-5.4)	3.0 (1.2-4.8)	0.737
Arousal	2.55 (0-5.7)	3.0 (0-5.1)	0.344
Lubrication	3.0 (0-4.5)	3.3 (0-4.5)	0.249
Orgasm	2.0 (0-6)	3.8 (0-6)	0.132
Satisfaction	4.6 (0.8-6)	3.8 (0.4-6)	0.263
Pain	3.2 (0-6)	4.2 (0-6)	0.165
FSFI Total score	18.65 (2-32.4)	22.6 (2.4-30.8)	0.086
Quality of life score (SF 36)			
Physical functioning	55 (10-100)	65 (10-95)	0.077
Physical role challenge	0 (0-100)	25 (0-100)	0.492
Emotional role difficulty	33.33 (0-100)	16.66 (0-100)	0.138
Energy/vitality	45 (5-95)	40 (0-90)	0.101
Mental health	60 (12-100)	56 (28-88)	0.135
Social functionality	62.5 (0-100)	62.5 (0-100)	0.952
Bodily pain	45 (0-100)	45 (0-77.50)	0.968
General perception of health	45 (0-90)	32.5 (0-85)	0.068
Hospital Depression/Anxiety Scale			
Depression score	7 (0-21)	7 (0-17)	0.915
Anxiety score	7 (0-21)	7 (1-17)	0.505

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FSFI: Female Sexual Function Index; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire; HLA B27: human leukocyte antigen B27; Anti TNF: anti-tumour necrotising factor. Values given as median (min-max).

numerical variables was evaluated with the Kolmogorov-Smirnov test, and the comparison of the variances between the groups was evaluated with the Levene test. The difference between the numerical variables of the two groups was analysed using the t-test as a parametric test and the Mann-Whitney U-test as a non-parametric test. Categorical variables were compared using the chi-square test. The correlation between variables was evaluated with the Spearman or Pearson correlation coefficient. A *p*-value of less than 0.05 was considered statistically significant. Multivariable logistic regression models were created to determine independent predictors of low FSFI score. The likelihood of association between low FSFI score and various evaluated parameters is reported as odds ratios (OR) ± 95% confidence interval (CI). Goodness of model fit was assessed by Hosmer-Lemeshow Test (24).

The mean total FSFI score in Turkish women was reported to be 25 (15). We estimated a need for at least 93 subjects in each group to test for a 5% decrease from 25% in controls to 20% in SPA patients with 90% power (significance level=0.05, one-tailed).

Table III. Pearson's correlation analysis between the FSFI scores and investigated variables among the patients with axSpA.

	Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain	FSFI Total Score
Age	-0.152*	-0.283**	-0.317*	-0.296**	-0.262**	-0.224**	-0.300**
BMI	-0.049	-0.029	-0.112*	-0.067	-0.132*	-0.091	-0.107
Gravida	-0.194*	-0.131*	-0.189*	-0.155*	-0.125*	-0.139*	-0.175*
Parity	-0.234**	-0.210**	-0.202**	-0.224**	-0.162*	-0.130*	-0.216**
C/S birth history	0.195*	0.156*	0.116*	0.151*	0.148*	0.031	0.143*
Smoking	-0.086	0.038	0.061	0.070	-0.072	0.023	0.016
Education	-0.191*	0.247*	0.131*	0.232*	0.117*	-0.127*	0.203*
Age of menarche	-0.058	-0.035	-0.124*	-0.065	-0.124*	-0.194*	-0.121*
Duration of menopause	-0.245**	-0.355**	-0.395**	-0.357**	-0.292**	-0.271**	-0.369**
Clitoral atrophy	-0.306**	-0.322**	-0.409**	-0.325**	-0.284**	-0.269**	-0.365**
Labial atrophy	-0.347**	-0.248**	-0.335**	-0.279**	-0.267**	-0.276**	-0.329**
Vaginal atrophy	-0.274**	-0.267**	-0.316**	-0.261**	-0.225**	-0.218**	-0.295**
Feeling of dryness in vagina	-0.070	-0.122*	-0.194*	-0.157*	-0.103*	-0.129*	-0.153*
Cervical atrophy	-0.293**	-0.335**	-0.399**	-0.331**	-0.283**	-0.296**	-0.371**
Speculum pain score	-0.241**	-0.285**	-0.370**	-0.339**	-0.326**	-0.387**	-0.380**
Vaginal infection	0.052	0.065	0.090	0.045	0.005	0.001	0.047
Atrophy in smear	-0.120*	-0.168*	-0.230**	-0.150*	-0.149*	-0.171*	-0.192*
Duration of diseases	-0.257*	-0.299*	-0.289*	-0.324*	-0.286*	-0.288*	-0.312*
CRP	0.129	0.097	0.071	-0.067	0.122	-0.002	0.051
ESR	-0.136	-0.069	-0.127	-0.135	-0.118	-0.139	-0.129
Enthesitis score	-0.119	-0.118	-0.146	-0.127	0.008	-0.134	-0.112
VAS	-0.122	-0.093	-0.061	-0.085	-0.006	-0.099	-0.080
HAQ	-0.105	-0.144	-0.244*	-0.145	-0.085	-0.206*	-0.169
HLA B27 positivity	-0.122	-0.143	-0.074	-0.099	-0.168	-0.067	-0.117
BASDAI	-0.056	0.070	0.096	0.156	0.131	0.173	0.118
BASMI	0.021*	0.008*	0.059*	0.018*	0.095*	0.015*	0.031*
BASFI	-0.257	-0.338	-0.356	-0.348	-0.279	-0.316	-0.339
Fatigue score	-0.051	0.013	0.073	0.026	0.088	0.017	0.035
Use of A-TNF/SLZ	-0.126	-0.071	-0.085	-0.116	-0.097	-0.124	-0.111

BMI: body mass index; C/S: Cesarean section; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FSFI: Female Sexual Function Index; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire; HLA B27: human leukocyte antigen B27; Anti TNF: anti-tumour necrotising factor; SLZ: Salazopyrin. *p<0.05; **p<0.001.

Results

Ninety-eight patients with axSpA and 99 controls were included in the study. Age, gravida and parity, previous births, BMI, and smoking and education status of the patients did not differ between the two groups (p>0.05). The number of postmenopausal patients and the duration of menopause were similar in both groups. Clitoral and labial atrophy and speculum pain score were significantly higher in the axSpA group (p<0.05). The clinical and demographic characteristics of the patients and healthy controls are listed in Table I. The FSFI and QoL-SF-36 scores were significantly lower (Fig. 1-2) and HADS scores were significantly higher in the axSpA group than in the control group (Fig. 3) (p<0.05).

There was no significant difference between the axSpA subgroups in terms of the FSFI, QoL-SF-36 and HAD scores (Table III). However, age, age at diagnosis, disease duration, serum CRP levels, HLA B27 positivity, BASMI, BASFI, and drug use significantly differed between the two axSpA groups (p<0.05) (Table II).

The correlation between the sexual function scores with other data and regression coefficients at 95% confidence interval were determined for the axSpA and control groups. While the gynaecological examination findings had a significant correlation with FSFI scores, no significant correlation was determined between sexual function and disease-related variables, except BASMI (Table III). Clitoral and labial atrophy was strongly correlated with the patients' age, duration of menopause, and axSpA duration (p<0.001). In addition, atrophy in the smear was significantly higher in patients with labial atrophy and clitoral atrophy (p<0.05). A significant correlation was also shown for the QoL measures in eight areas with sexual desire, arousal, lubrication, orgasm, satisfaction, pain and total FSFI scores. HADS-A measures had a significant correlation with all sexual functions but orgasm, while the HADS-D measures were significantly correlated only with sexual desire and satisfaction (Table IV).

We performed logistic regression analysis in the model assuming FSFI total value of <23 for sexual dysfunction (25) and after correcting for age, parity, duration of menopause, menopausal status and mode of delivery, the presence of axSpA was found independently associated to sexual disorder (OR 3.002, 95% CI 1.629–5.531, p<0.001) (Table V). In addition, this analysis ad-

Table IV. Pearson's correlation analysis of the FSFI scores with the SF-36 Quality of Life Scale and HADS scores of the patients with axSpA.

	Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain	FSFI total score
Quality of life score (SF-36)							
Physical Functioning	0.355**	0.248**	0.340**	0.261**	0.282**	0.248**	0.324**
Physical role challenge	0.317**	0.175**	0.248**	0.163*	0.135*	0.142*	0.214**
Emotional role difficulty	0.255**	0.118*	0.151*	0.138*	0.206**	0.131*	0.182**
Energy/vitality	0.238**	0.101*	0.077	0.055	0.170*	0.027	0.113*
Mental health	0.304**	0.146*	0.087	0.132*	0.243**	0.087	0.175*
Social functionality	0.287**	0.109*	0.142*	0.113*	0.180**	0.107*	0.166*
Bodily pain	0.275**	0.177*	0.283**	0.200**	0.228**	0.241**	0.265**
General perception of health	0.254**	0.173*	0.133*	0.150*	0.252**	0.182*	0.211**
Hospital Depression/Anxiety Scale							
Depression score	-0.116*	-0.010	-0.013	0.016	-0.133*	-0.001	-0.039
Anxiety score	-0.261**	0.151*	-0.100*	-0.090	-0.236*	0.006*	-0.143*

FSFI: Female Sexual Function Index; SF-36: Short Form-36; axSpA: axial spondyloarthropathy. *p<0.05; **p<0.001.

Table V. Logistic regression analysis demonstrating predictors of low FSFI score.

	OR (95% CI)	p
Parity	1.470 (1.053-2.051)	0.024
Presence of axSpA	3.002 (1.629-5.531)	<0.001
Menopause status	2.900 (1.569-5.361)	0.001

Analyses adjusted for age, parity, presence of axSpA, menopause status and mode of delivery. FSFI: Female Sexual Function Index; axSpA: axial spondyloarthropathy; OR: odds ratio; 95% CI: 95% confidence interval.

justed for age, menopausal status and mode of delivery, duration of disease and BASMI in the subgroups, and it revealed that the duration of the disease was independently associated with sexual dysfunction (OR 1.283, 95% CI 1.035–1.591, p=0.023).

Discussion

All the domains of sexual activity may be affected by rheumatic diseases (8). In our study, all of the FSFI domain scores were significantly lower in patients with axSpA compared with the healthy controls. We do not yet have sufficient data on whether this is the primary effect of the disease or the consequence of mental and physical fatigue due to the disease. The difference of this study from previous research is that each patient underwent a gynaecological evaluation, through which we determined that labial and clitoral atrophy and speculum pain score were significantly higher in women with axSpA. The major cause of urogenital atrophy in menopausal women is estrogen loss. The reduction of estrogen level causes a decrease in the blood supply of the urogenital area and a decrease in the tension of supporting musculofascial structures in the pelvic area (26, 27). The atrophic changes of the vulva, vagina and lower urinary tract can have a large impact on the QoL of menopausal women. Paravertebral muscle atrophy has been previously reported in patients with AS presenting with lumbar pain (28). Resorlu *et al*. suggested that chronic inflammation, cytokine-mediated fibrosis, immobilisation, and postural changes in AS contributed to fatty degeneration and atrophy in paravertebral muscles (29). The strong correlation between axSpA duration and genital atrophy suggests that with the prolongation of chronic process, inflammation and cytokine mediated fibrosis may also play a role in fatty degeneration and atrophy of the urogenital area. Considering that urogenital atrophy increases with increasing age and shows a strong correlation with the duration of menopause, it suggests that axSpA duration may contribute to the development of atrophy. Although it can be speculated that axSpA may cause genital atrophy, especially labial and clitoral, further studies involving broader and more objective definitions are required since in our study, the atrophy evaluation was subjectively performed by the same gynaecologist.

Chronic arthritis including SpA has a significant effect on patients' emotional and physical status (8, 30). A healthy mental state is an important issue in terms of healthy sexual functioning. A great number of studies have shown a correlation between sexual dysfunction and depression in AS patients (9, 30, 31). Sarıyıldız *et al*. found no significant correlation between HADS-A and HADS-D levels and FSFI (32). In the current study, while there was no significant correlation between depression scores and sexual functions except sexual desire, the anxiety score had a significant correlation with all sexual domains except orgasm.

Pain or limitation caused by SpA can negatively affect QoL, as well as sexual dysfunction. QoL is strongly correlated with sexual function in female patients with AS (33). However, there is only a limited number of studies evaluating the effects of QoL on sexual function in SpA patients (9, 32-34). In our study, all the QoL measures were significantly lower in women with axSpA compared to the healthy women, and they were also strongly correlated with all the domains of sexual function in all participants.

Mobility problems in the joints, especially the hip joint and spine, can be seen in patients with AS, and this limitation may cause sexual dysfunction by making certain positions difficult. BASMI is the main assessment for the measurement of mobility in axSpA patients. There are studies reporting conflicting results concerning the relationship between BASMI and sexual function. While some researchers showed that joint mobility affected sexual function in AS patients (8, 9, 34), others found no such correlation between BASMI and sexual dysfunction (32, 35). In our study, a correlation was observed between the BASMI and

FSFI scores, and BASMI also had a strong correlation with age and axSpA duration; furthermore, sexual functions were strongly correlated with both of these variables. However, we did not find any significant relationship between the determinant variables of the disease and sexual functions. This suggests that limited mobility may cause sexual dysfunction in female AS patients, especially among those with a longer disease duration. It can be suggested that long-lasting axSpA causing limitations on movement affects sexual functions more than active disease. In a very recent study, when the burden of the disease was measured using the Assessment of SpondyloArthritis international Society-Health Index (ASAS-HI), it was revealed that BASDAI and Ankylosing Spondylitis Disease Activity Score-C-Reactive Protein (ASDAS-CRP) was independently associated to the response for the item involving sexual function (36). On the contrary, although the presence of axSpA and the duration of the disease were found independently associated to sexual dysfunction in our study, an independent association was not shown with the disease variables.

In the current study, we confirmed the presence of a similar burden of disease activity measured by BASDAI for the patients with AS and nr-axSpA. However, functional limitation (BASFI) and spinal mobility (BASMI) were less impaired in patients with nr-axSpA compared to those with AS. As in previous studies (35, 37, 38), the nr-axSpA population enrolled in this study was younger than the AS population. This is the first study assessing sexual function in axSpA and comparing patients with AS and nr-axSpA, and the results revealed that sexual function did not significantly differ between the AS and nr-axSpA subgroups. Kilic *et al*. showed no major differences concerning the risk of anxiety and depression between the patients with AS and nr-axSpA (39), and we confirmed these findings in our study.

One of the limitations of the study is that only sexually active women were included in the study. Furthermore, since sexuality cannot be questioned easily and sexual health is often neglected, we do not know how many of the patients that claimed to be sexually active were actually so. We should consider the participants' responses concerning sexuality from this perspective. Another limitation of our study is that although the clinician who performed the gynaecological examination had sufficient experience, the atrophy decision was based on a subjective evaluation. We tried to compensate for this limitation by detecting atrophy with a cervicovaginal smear.

In conclusion, in women with axSpA, especially among the elderly, the disease duration and limitation of movement have statistically significant detrimental effects on sexual functions, causing increased genital atrophy. The sexual functions and physical burden of the disease do not differ between women with AS and nr-axSpA.

References

1. ZOCHLING J, SMITH EU: Seronegative spondyloarthritis. *Best Pract Res Clin Rheumatol* 2010; 24: 747-56.
2. RUDWALEIT M, HAIBEL H, BARALIAKOS X *et al*.: The early disease stage in axial spondyloarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Rheum* 2009; 60: 717-27.
3. BURGOS-VARGAS R, BRAUN J: Inflammatory back pain. *Rheum Dis Clin North Am* 2012; 38: 487-99.
4. WEISMAN MH: Inflammatory back pain: the United States perspective. *Rheum Dis Clin North Am* 2012; 38: 501-12.
5. ROBINSON PC, WORDSWORTH BP, REVEILLE JD, BROWN MA: Axial spondyloarthritis: a new disease entity, not necesssarily early ankylosing spondylitis. *Ann Rhuem Dis* 2013; 72: 162-4.
6. ROBINSON PC, BROWN MA: The genetics of ankylosing spondylitis and axial spondyloarthritis. *Rheum Dis Clin North Am* 2012; 38: 539-53.
7. SIEPER J, VAN DER HEIJDE D, DOUGADOS M *et al*.: Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). *Ann Rheum Dis* 2013; 72: 815-22.
8. CAKAR E, DINCER U, KIRALP MZ *et al*.: Sexual problems in male ankylosing spondylitis patients: relationship with functionality, disease activity, quality of life, and emotional status. *Clin Rheumatol* 2007; 26:1607-13.
9. AKKURT HE, YILMAZ H, YILMAZ S, PARLAK L, ORDAHAN B, SALLI A: Evaluation of sexual dysfunction in females with ankylosing spondylitis. *Arch Rheumatol* 2016; 31: 41-7.
10. YILMAZ H, YILMAZ SD, POLAT HA, SALLI A, ERKIN G, UGURLU H: The effects of fibromyalgia syndrome on female sexuality: a controlled study. *J Sex Med* 2012; 9: 779-85.
11. BLAKE DJ, MAISIAK R, ALARCON GS, HOLLEY HL, BROWN S: Sexual quality-of-life of patients with arthritis compared to arthritis-free controls. *J Rheumatol* 1987; 14: 570-6.
12. PIGG JS, SCHROEDER PM: Frequently occurring problems of patients with rheumatic diseases. The ANA outcome standards for rheumatology nursing practice. *Nurs Clin North Am* 1984; 19: 697-708.
13. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R *et al*.: The Development of Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011; 70: 25-31.
14. ROSEN R, BROWN C, HEIMAN J *et al*.: The Female Sexual Dysfunction Index (FSFI): a multidimensional self-report instrumentfor the assessment of female sexual function. *J Sex Marital Ther* 2000; 26: 191-208.
15. ÖKSÜZ E, MALHAN S: Prevalence and risk factors for female sexual dysfunction in Turkish women. *J Urol* 2006; 175: 654-8.
16. SULLIVAN M, KARLSSON J: The Swedish SF-36 Health Survey III. Evaluation of criterion-based validity: results from normative population. *J Clin Epidemiol* 1998; 51: 1105-13.
17. PERSSON LO, KARLSSON J, BENGTSSON C, STEEN B, SULLIVAN M: The Swedish SF-36 Health Survey II. Evaluation of clinical validity: results from population studies of elderly and women in Gothenborg. *J Clin Epidemiol* 1998; 51: 1095-103.
18. ZIGMOND AS, SNAITH RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361-70.
19. AYDEMIR O, GUVENIR T, KUEY L, KULTUR S: Validity and reliability of Turkish version of hospital anxiety and depression scale. *Turk Psikiyatri Derg* 1997; 8: 280-7.
20. AKKOC Y, KARATEPE AG, AKAR S, KIRAZLI Y, AKKOC N: A Turkish version of the Bath Ankylosing Spondylitis Disease Activity Index: reliability and validity. *Rheumatol Int* 2005; 25: 280-4.
21. DALTROY LH, LARSON MG, ROBERTS NW, LIANG MH: A modification of the Health Assessment Questionnaire for the spondyloarthropathies. *J Rheumatol* 1990; 17: 946-50.
22. SIEPER J, RUDWALEIT M, BARALIAKOS X *et al*.: The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis* 2009; 68: 1-44.
23. HILDEN M, SIDENIUS K, LANGHOFF-ROOS J, WIJMA B, SCHEI B: Women's experiences of the gynecologic examination: factors associated with discomfort. Acta Obstetricia at Gynecologica Scandinavia 2003; 82: 1030-6.
24. HOSMER DW, LEMESHOW S: Applied Logistic Regression, Second Edition, New York: John Wiley & Sons, 2000.
25. CLAYTON AH, SEGRAVES RT, LEIBLUM S *et al*.: Reliability and validity of the Sexual Interest and Desire Inventory-Female (SIDI-F), a scale designed to measure severity of female hypoactive sexual desire disorder. *J Sex Marital Ther* 2006; 32: 115-35.
26. CALLEJA-AGIUS J, BRINCAT MP: Urogenital atrophy. *Climacteric* 2009; 12: 279-85.
27. AMSTERDAM A, KRYCHMAN M: Clitoral atrophy: a case series. *J Sex Med* 2009; 6: 584-7.

28. KANG CH, SHIN MJ, KIM SM, LEE SH, LEE CS: MRI of paraspinal muscles in lumbar degenerative kyphosis patients and control patients with chronic low back pain. *Clin Radiol* 2007; 62: 479-86.
29. RESORLU H, SAVAS Y, AYLANC N, GOKMEN F: Evaluation of paravertebral muscle atrophy and fatty degeneration in ankylosing spondylitis. *Mod Rheumatol* 2017; 27: 683-7.
30. MICHAEL A, O'KEANE V: Sexual dysfunction in depression. *Hum Psychopharmacol* 2000; 15: 337-45.
31. ELST P, SYBESMA T, VAN DER STADT RJ, PRINS APA, HISSINK MULLER W, DEN BUTTER A: Sexual problems in rheumatoid arthritis and ankylosing spondylitis. *Arthritis Rheum* 1984; 27: 217-20.
32. SARIYILDIZ MA, BATMAZ I, INANIR A *et al*.: The impact of ankylosing spondylitis on female sexual functions *Int J Impot Res* 2013; 25: 104-8
33. ABDEL-NASSER AM, ALI EI: Determinants of sexual disability and dissatisfaction in female patients with rheumatoid arthritis. *Clin Rheumatol* 2006; 25: 822-30.
34. DEMIR SE, REZVANI A, OK S: Assessment of sexual functions in female patients with ankylosing spondylitis compared with healthy controls. *Rheumatol Int* 2013; 33: 57-63.
35. BAL S, BAL K, TURAN Y *et al*.: Sexual functions in ankylosing spondylitis. *Rheumatol Int* 2011; 31: 889-94.
36. RUDWALEIT M, HAIBEL H, BARALIAKOS X *et al*.: The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Rheum* 2009; 60: 717-27.
37. QUEIRO R, ALONSO S, MORANTE I, ALPERI M: Sexual disinterest in spondyloarthritis patients. Comparison between psoriatic arthritis and axial spondyloarthritis using a sexuality-specific question from the ASAS Health Index. *Clin Exp Rheumatol* 2021 Feb 15 PMID 33635216 [Online ahead of print].
38. KILTZ U, BARALIAKOS X, KARAKOSTAS P *et al*.: Do patients with nonradiographic axial spondylarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res* 2012; 64: 1415-22.
39. KILIC E, KILIC G, AKGUL O *et al*.: Discriminant validity of the Ankylosing Spondylitis Disease Activity Score (ASDAS) in patients with non-radiographic axial spondyloarthritis and ankylosing spondylitis: a cohort study. *Rheumatol Int* 2015; 35: 981-9.
40. KILIC G, KILIC E, OZGOCMEN S: Relationship between psychiatric status, self-reported outcome measures, and clinical parameters in axial spondyloarthritis. *Medicine* 2014; 93: e337.