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Gender differences in clinical features and quality of life of patients with axial spondyloarthritis and psoriatic arthritis

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SUMMARY

Objective. The aim of the current study was to compare the clinical and treatment characteristics and dimensions of health-related quality of life between female and male patients with axial spondyloarthritis (SpA) and psoriatic arthritis (PsA).

Methods. The present study is cross-sectional and comprises 119 patients with axial SpA and 198 patients with PsA. Clinical data were collected by standardized and self-reported instruments. Disease activity was evaluated by the Ankylosing Spondylitis Disease Activity Score with C-reactive protein and the Disease Activity in PSoriatic Arthritis (for SpA and PsA, respectively). Health-related quality of life was assessed with the Medical Outcomes Study 36-item Short Form Survey. Patients were stratified by gender, and the socio-demographic, clinical, and quality-of-life data were compared.

Results. Women with axial SpA and PsA had significantly lower education ($p<0.001$, $p=0.004$, respectively) and higher disease activity ($p<0.001$, $p=0.003$, respectively). Female patients with axial SpA were more frequently under second-line therapy ($p=0.026$) and glucocorticoid treatment ($p=0.005$), while women with PsA had more radiographic progression ($p=0.006$). Female patients with axial SpA and PsA had worse scores in the dimensions of quality of life regarding physical role, bodily pain, vitality, and mental health. Women with axial SpA had lower scores in general health, while women with PsA had lower scores in physical and social functioning.

Conclusions. Women with axial SpA and PsA had worse scores than men in most clinical and treatment characteristics and health-related quality of life dimensions.

***Key words**: Axial spondyloarthritis, psoriatic arthritis, gender, health-related quality of life, disease activity.*

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INTRODUCTION

Gender differences are a relevant and substantial source of variation in a number of clinical and subclinical conditions, affecting risk factors, prevalence, age of onset, clinical presentation, symptomatology, prognosis, and treatment effectiveness. Since disease experience and responses to therapeutic interventions are often significantly different in women compared to men (1), personalized preventive and therapeutic strategies are being sought, taking into account gender differences (2).

A group of inflammatory rheumatic diseases, such as axial spondyloarthritis (SpA) and psoriatic arthritis (PsA), affects male and female patients differently, giving rise to divergent clinical presentation, disease course, and response to treatment (3, 4).

Considering clinical features, female patients with axial SpA have a higher disease burden due to a longer diagnostic delay, a higher disease activity, and a lower efficacy of treatment, but male patients have more radiographic damage (5). Women with PsA tend to have worse functioning, a higher disease burden (6), a higher number of swollen joints, and an increased functional disability score than men (7). Due to the diverse nature of the disease, understanding how gender influences disease outcomes will help clinicians optimally tailor management strategies for individual patients

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(8) and increase patients' quality of life.
Health-related quality of life (HRQoL) is a self-administered questionnaire that quantifies how health status affects the quality of life, specifically the self-perceived well-being related to the presence of the disease or treatment (9). Patients with axial SpA had a substantially lower HRQoL than the general population (10), while gender-based differences in axial SpA are vague. In some studies (11, 12), women had the worst quality of life, and in other studies (13-15), scores tended to be similar in both genders, while in one study (16), male patients had lower scores. The impaired HRQoL reported in women with axial SpA can be explained by outcomes such as fatigue, pain, sleep disturbances, and increased disease activity, all of which have been shown to affect women more than men (17). Patients with PsA experienced reduced quality of life in comparison to the general population (18), and women with PsA often experienced worse quality of life, higher pain, fatigue, and functional disability than men (4, 19).
The existence of gender differences in HRQoL is strongly influenced by the methodology of the study, specifically whether data collection is done at baseline or over time (3), whether HRQoL's physical or mental aspect is evaluated (12), and by the measure of quality of life that has been used (12).
To our knowledge, there are few studies analyzing gender differences in clinical characteristics and HRQoL in both axial SpA and PsA. Therefore, the present study aims to compare: i) the sociodemographic and clinical features; and ii) the dimensions of HRQoL between female and male patients with axial SpA and PsA. Specifically, we hypothesized that women with both axial SpA and PsA have a more severe disease activity and, consequently, a more aggressive therapy and a reduced HRQoL.

MATERIALS AND METHODS

Study design and clinical sample

This observational, cross-sectional study included patients with axial SpA and PsA. All patients were 18 years of age or older, clinically stable, and already diagnosed with axial SpA, according to the Assessment of Spondyloarthritis International Society classification criteria (20), or PsA, according to the Classification criteria for Psoriatic ARthritis criteria (21). Exclusion criteria included a diagnosis of fibromyalgia, connective tissue diseases (systemic lupus erythematosus, Sjögren's syndrome, scleroderma, dermatomyositis, polymyositis), vasculitis, gout, infective arthritis, polymyalgia rheumatica, or other severe systemic diseases. Recruitment was done during a routine outpatient visit at the Unit of Rheumatology, University Hospital of Verona, during a period of one year (22-24).

Measurements

Clinical data were collected using standardized tools. Disease activity was assessed by the Ankylosing Spondylitis Disease Activity Score with C-Reactive Protein (ASDAS-CRP) in the patients with axial SpA (25), and by the Disease Activity in PSoriatic Arthritis (DAPSA) in the patients with PsA (26). Disease duration, comorbidity, familial predisposition, body mass index, erosions, and radiographic progression were also recorded. Rheumatological treatment was categorized as first-line therapy [conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or anti-tumor necrosis factor (anti-TNF) drugs] and second-line therapy [biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs with or without DMARDs] according to Tosato *et al.* (27). The use of glucocorticoids and non-steroidal anti-inflammatory drugs (NSAIDs) was also recorded. HRQoL was evaluated using the self-reported Medical Outcomes Study 36-item Short Form Survey (SF-36; Italian version) (28). The instrument assesses eight dimensions of health status: physical functioning (PF), role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. Lower scores on each dimension indicate a worse HRQoL (29). Previous studies confirm the SF-36 as a valid and reliable measure of HRQoL for

patients with SpA and PsA at a single time point (30, 31).

Statistical analysis

The characteristics were presented as frequencies (%) for categorical variables and means [standard deviations (SD)] for continuous variables. Comparisons between females and males within the two diagnostic groups of axial SpA and PsA were performed using Fisher's exact test (two categories), Chi-square test (> two categories) for categorical variables, and *t*-test (independent samples) for continuous variables. All tests were bilateral, with a significant level at 0.05. Statistical analyses were performed using SPSS 22 (IBM, Armonk, NY, USA) for Windows.

RESULTS

A total of 119 patients with axial SpA (54 females and 65 males) and 198 with PsA (124 females and 74 males) were assessed. Socio-demographic characteristics of women and men are presented in Table I.

The mean age was not significantly different between male and female patients, as were marital status and education. Instead, female patients were less frequently employed, both in axial SpA (females 61.1% *versus* males 87.7%; p=0.001), and in PsA (females 44.4% *versus* males 64.9%; p=0.006).

Table II shows clinical and treatment characteristics in axial SpA and PsA, compared by gender. In both axial SpA and PsA, disease activity was higher in female patients (ASDAS-CRP females 2.9 SD 1.0 *versus* males 2.2 SD 1.1; p<0.001; DAPSA females 16.6 *versus* males 12.8; p=0.003). Disease duration (in years) was shorter in female patients with PsA (females 8.1 SD 7.0 *versus* males 10.1 SD 6.7; p=0.048), while in patients with axial SpA, there was no difference (p=0.083). Considering comorbidity, familial predisposition, body mass index, and erosion, female and male patients were similar.

Female patients with axial SpA were more frequently assuming second-line therapy (p=0.043) and glucocorticoids (p=0.006). Conversely, gender differences were not seen for NSAID treatment (p=0.710). Female and male patients with PsA were similar in treatment characteristics.

As shown in Figure 1, female patients had lower scores in most dimensions of quality of life. Considering patients with axial SpA, females had lower scores in three out of four dimensions of physical quality of life, specifically in role limitation due to physical health (p=0.004), bodily pain (p=0.006), and general health (p=0.011). In two out of four dimensions of mental quality of life, females had lower scores, specifically in vitality (p<0.001) and mental health (p=0.022). Considering PsA, female pa-

Table I - Socio-demographic characteristics of the patients with axial spondyloarthritis and psoriatic arthritis, compared by gender.

	Axial spondyloarthritis (n=119)			Psoriatic arthritis (n=198)		
Socio-demographic characteristics	**Females (n=54)**	**Males (n=65)**	**p**	**Females (n=124)**	**Males (n=74)**	**p**
Age (years), mean (SD)	51.1 (12.1)	47.2 (11.1)	0.072[c]	57.3 (11.5)	56.1 (12.0)	0.481[c]
Marital status, n (%) Single Married Separated/Divorced/Widowed	 9 (16.7) 42 (77.8) 3 (5.6)	 17 (26.2) 44 (67.7) 4 (6.2)	0.439[b]	 13 (10.5) 93 (75.0) 18 (14.5)	 10 (13.5) 59 (79.7) 5 (6.8)	0.234[b]
Education, n (%) Low High	 18 (33.3) 36 (66.7)	 27 (37.8) 38 (58.5)	0.233[b]	 67 (54.0) 57 (46.0)	 36 (48.6) 38 (51.4)	0.279[a]
Employment, n (%) No Yes	 21 (38.9) 33 (61.1)	 8 (12.3) 57 (87.7)	<0.001[a]	 69 (55.6) 55 (44.4)	 26 (35.1) 48 (64.9)	0.004[a]

SD, standard deviation; [a]Fisher's exact test; [b]Chi-square test; [c]*t*-test.

Table II - Clinical and treatment characteristics of the patients with axial spondyloarthritis and psoriatic arthritis, compared by gender.

	Axial spondyloarthritis (n=119)			Psoriatic arthritis (n=198)		
Clinical characteristics	**Females (n=54)**	**Males (n=65)**	**p**	**Females (n=124)**	**Males (n=74)**	**p**
Disease activity						
ASDAS-CRP, mean (SD)	2.9 (1.0)	2.2 (1.1)	<0.001[c]			
Inactive (<1.3), n (%)	6 (11.1)	15 (23.1)	0.012[b]			
Moderate (≥1.3 and <2.1), n (%)	6 (11.1)	17 (26.2)				
High (≥2.1 and ≤3.5), n (%)	26 (48.1)	25 (38.5)				
Very high (>3.5), n (%)	16 (29.6)	8 (12.3)				
DAPSA, mean (SD)				16.6 (9.5)	12.8 (7.0)	0.003[c]
Remission (≤4), n (%)				7 (5.6)	5 (6.8)	0.033[b]
Low (>4 and ≤14), n (%)				47 (37.9)	42 (56.8)	
Moderate (>14 and ≤28), n (%)				55 (44.4)	24 (32.4)	
High (>28), n (%)				15 (12.1)	3 (4.1)	
Disease duration, mean (SD), years	8.6 (7.3)	11.2 (8.8)	0.083[c]	8.1 (7.0)	10.1 (6.7)	0.048[c]
Comorbidity, n (%)						
No	6 (11.1)	14 (21.5)	0.101[a]	14 (11.3)	5 (6.8)	0.215[a]
Yes	48 (88.9)	51 (78.5)		110 (88.7)	69 (93.2)	
Familiarity, n (%)						
No	41 (75.9)	46 (70.8)	0.337[a]	79 (63.7)	53 (71.6)	0.162[b]
Yes	13 (24.1)	19 (29.2)		45 (36.3)	21 (28.4)	
BMI, mean (SD)	25.4 (5.7)	26.2 (2.9)	0.301[c]	26.2 (5.0)	27.1 (3.6)	0.200[c]
Erosion, n (%)						
No	48 (88.9)	61 (93.8)	0.261[a]	102 (82.3)	63 (85.1)	0.375[a]
Yes	6 (11.1)	4 (6.2)		22 (17.7)	11 (14.9)	
Radiographic progression, n (%)						
No	27 (50.0)	41 (63.1)	0.106[a]	58 (46.8)	49 (66.2)	0.006[a]
Yes	27 (50.0)	24 (36.9)		66 (53.2)	25 (33.8)	
Treatment characteristics						
Rheumatological treatment, n (%)						
First-line therapy[1]	41 (75.9)	59 (90.8)	0.026[a]	97 (78.2)	58 (78.4)	0.564[a]
Second-line therapy[2]	13 (24.1)	6 (9.2)		27 (21.8)	16 (21.6)	
Glucocorticoid treatment, n (%)						
No	37 (68.5)	58 (89.2)	0.005[a]	91 (73.4)	62 (83.8)	0.063[a]
Yes	17 (31.5)	7 (10.8)		33 (26.6)	12 (16.2)	
NSAID treatment[3], n (%)						
No	33 (61.1)	37 (56.9)	0.392[a]	84 (67.7)	52 (70.3)	0.418[a]
Yes	21 (38.9)	28 (43.1)		40 (32.3)	22 (29.7)	

SD, standard deviation; ASDAS-CRP, ankylosing spondylitis disease activity score with C-reactive protein; DAPSA, disease activity in psoriatic arthritis; BMI, body mass index; NSAID treatment, non-steroidal anti-inflammatory drug treatment; [1]conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or anti-tumor necrosis factor drugs; [2]anti- interleukin-6/ biological disease-modifying antirheumatic drugs/ targeted synthetic disease-modifying antirheumatic drugs with or without csDMARDs; 3used in the last ten days; [a]Fisher's exact test; [b]Chi-square test; [c]*t*-test.

tients had lower scores in three out of four dimensions of physical quality of life: PF (p<0.001), role limitations due to physical health (p=0.009), and bodily pain (p<0.001). As regards mental quality of life, females had lower scores than males in three of four dimensions: vitality (p=0.012), social functioning (p=0.001), and mental health (p=0.004).

DISCUSSION AND CONCLUSIONS

The results of the present study indicate two main findings: i) worse clinical and treatment features; and ii) lower quality of life in female patients with axial SpA and PsA. These results confirmed the proposed hypothesis of more severe disease activity,

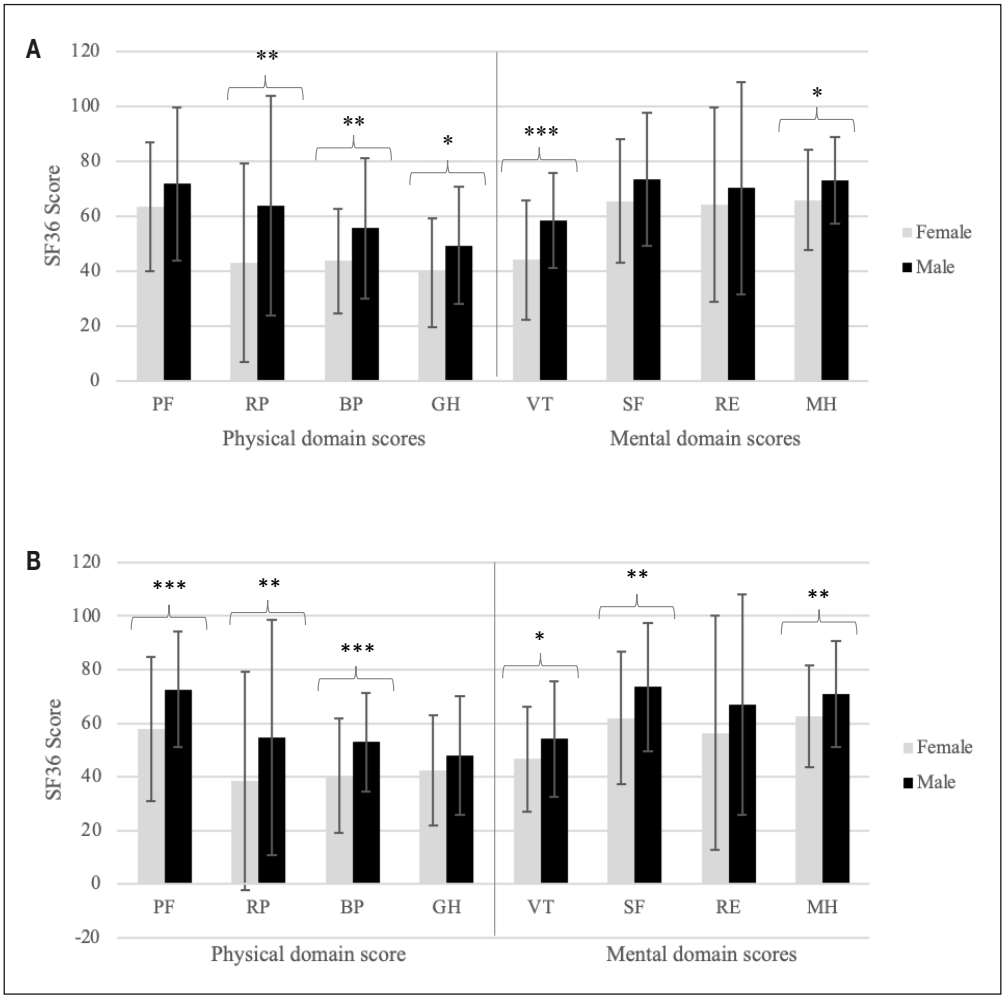

Figure 1 - Physical and mental domains of health-related quality of life [short form-36 (SF-36)] in axial spondyloarthritis (females n=54; males n=65) (a), and psoriatic arthritis (females n=124; males n=74) (b), compared by gender. Mean and standard deviation are shown. The SF-36 domains score between 0 and 100 (0: worse health; 100: best health). *T*-test is used to compare gender differences. PF physical functioning; RP role limitations due to physical health; BP bodily pain; GH general health; VT vitality; SF social functioning; RE role limitations due to emotional problems; MH mental health. *p<0.05; **p<0.01; ***p<0.001.

more aggressive therapy, and reduced quality of life in women with axial SpA and PsA when compared to men.

The first main finding of the present study is the presence of worse clinical features in females, such as more severe disease activity in both axial SpA and PsA, more radiographic progression in PsA, and more frequent second-line therapy and glucocorticoid treatments. In particular, women with axial SpA and PsA had a higher level of perceived disease activity. Previous findings on axial SpA mostly showed the same results (14, 32), except in one study where gender differences in disease activity depended on the used measure (12). Indeed, women with PsA tended to report worse scores of disease activity (33). More severe disease activity in both women with axial SpA and PsA may be due to sex differences in immune mechanisms and to a greater disease burden due to the more extensive involvement of peripheral joints and entheses (3, 4, 12). Results of the present study showed that female and male patients with axial SpA had similar age and disease dura-

tion, while even though women and men with PsA did not differ in age, males had longer disease duration, indicating an older age at the diagnosis of PsA in females. This could be due to a biological difference between women and men, but it might also suggest delays in diagnosis, probably because of the misinterpretation of early symptoms of PsA in women (4).

In the present study, erosion and radiographic progression were not different between female and male patients with axial SpA, differently from previous studies, which found fewer radiologic abnormalities in women with axial SpA (3, 34, 35). Even with lower radiographic severity in females with axial SpA, after adjusting for radiographic spinal damage, women were found to report worse functioning at any given level of radiographic damage (36). In the current study, females with PsA were not different from males in the erosion of the bones but had significantly more radiographic progression. Previous studies found opposite results, where males with PsA were more likely to develop more severe radiographic structural damage (4, 7, 33) and a more erosive disease (4).

In the current study, a higher number of women with axial SpA were under second-line therapy, which is prescribed when the patients do not respond to first-line therapy, such as anti-TNF. Few studies have shown significantly poorer responses to TNF inhibitor therapies in women with axial SpA (14, 35). The present analysis did not find gender differences related to the rheumatological treatment of PsA patients. However, a previous study showed a higher response to anti-TNF at 6 months in men with PsA (4). The results of the present study showed that female axial SpA patients more often use glucocorticoids. This finding may be explained by worse disease activity in women, as short-term use of glucocorticoids is recommended to treat inflammation (37).

The second main finding in the current study is that the physical and mental dimensions of HRQoL were reduced in female patients with axial SpA and PsA. The higher disease activity in females with axial SpA and PsA could explain these differences since a previous study showed that female patients were more likely to report a high impact of disease activity on quality of life (32). In addition, it was found that the presence of pro-radiographic features in women with PsA could decrease their quality of life (7). Several studies have emphasized that women with axial SpA and PsA report a greater impairment in quality of life (4, 7, 8, 34, 35).

Considering specific dimensions of physical quality of life, PF is worse in female patients with PsA, as previously reported (38). Since a low score on the PF dimension is defined as being limited in performing all physical activities (29) and SF-36PF is the best instrument for measuring functional disability in PsA (39), the results of the present study are in line with previous findings, showing PsA women as more likely to have physical activity limitations (33). In the present study, in patients with axial SpA, the PF scores tend to be similar in both genders. Due to the progressive loss of spine mobility, physical limitations appear to be prevalent among axial SpA patients (10), but with conflicting results concerning gender differences, which range from a greater functional impairment in females to no gender differences (3). The dimension of the SF-36 role limitation due to physical health refers to problems with work or other daily activities because of physical health (29). In the present study, physical health was worse in females with axial SpA and PsA, and female patients were less often employed than male patients. Previous studies found that work disability associated with axial SpA and PsA occurs more often in women than in men of the same age (4, 10, 38), and that involvement of peripheral joints of the hands and feet, higher levels of pain, fatigue, and physical limitations could all contribute to it (4). One study recently showed that being employed was associated with a decreased probability of having low quality of life and depression in male patients with axial SpA (32). Previous papers highlighted that the educational level was strongly related to the type of job, and the work-disabled patients had a lower level of education, indirectly indicating that the

work-disabled patients might have more physically demanding jobs (8, 38). In the present study, there was no gender difference with respect to the level of education, thus suggesting that women's working capacity is reduced more by variables associated with the disease than by the level of education.

In the current study, bodily pain, another physical dimension in SF-36, was worse in female patients both in axial SpA and PsA (29). Pain is a substantial symptom of axial SpA and the most common complaint in patients (10). Women with axial SpA and PsA often report more intense pain and experience it at more sites, with a greater level of severity, a higher frequency, and a longer duration than men (3, 4, 8). Finally, women with axial SpA had lower scores on the dimension of general health, defining personal health as poor (29).

Considering the dimensions of mental quality of life, in the present study, lower scores in vitality were reported both in female patients with axial SpA and PsA than in their male counterparts. In SF-36, a low score on vitality is defined as a feeling of being tired and worn out (29), and SF-36 vitality is used to measure fatigue both in axial SpA and PsA (40, 41). Previous studies revealed that more than half of axial SpA patients reported fatigue induced by the disease (10), and in axial SpA and PsA women, the level of fatigue was higher compared to men (4, 8, 11). These results can be explained by higher physical limitations and mental dysfunction in women, as determined by SF-36 (7), and in the present study, these values were decreased. Mental health, a dimension of SF-36, was lower in female patients, both in axial SpA and PsA, which referred to higher individual feelings of anxiety and depression (10). In a previous study on axial SpA patients, the mental health dimension was reduced, suggesting that the impact of axial SpA on mental health was considerable (10). Results from a recent meta-analysis on axial SpA (42) showed that there were no differences in the risk of depression among men and women, while men have more than a two-fold increased risk for incident anxiety. Indeed, the risk of anxiety and depression is higher in women with PsA (4, 7, 8). Thus, the results of the present study suggest that a lower level of mental health in female patients can be due to the presence of depression and anxiety.

In the current study, women with PsA had lower scores on the dimension of social functioning since they more frequently felt interference with ordinary social activities due to physical and emotional problems (29).

The present study has several strengths. First, two inflammatory rheumatic diseases were considered, thus providing a broader perspective toward the understanding of gender-specific differences in arthritis. Second, the sample was composed of outpatients recruited during a routine visit without any restriction due to disease severity or treatment, enabling the findings to be generalizable to the axial SpA and PsA populations. A few limitations have to be mentioned. First, axial SpA was not considered in the categories of ankylosing spondylitis and non-radiographic axial SpA, even if previous research found clinical and quality of life differences between them (43). Contrarily, predominantly axial *versus* peripheral PsA was not significantly different in the dimensions of SF-36 (44). Second, the sample size was small when the axial SpA and PsA patients were stratified by gender, thus suggesting caution in data interpretation.

In conclusion, the present study revealed gender differences in clinical characteristics, treatment, and HRQoL in axial SpA and PsA, where women had worse scores in most of the variables. Quantifying the impact of disease on daily life in women and men is essential for developing an effective, precise, and gender-specific approach to these patients. The causes of gender differences in disease expression and outcomes are still unknown, but the presence of the differences supports the idea that working on appropriate rheumatological and psychological treatment targets according to gender could be the central point for improving the quality of life.

Contributions

BR, wrote the original draft; CB, performed the statistical analysis; MR, supervised the

recruitment, EF, recruited and assessed the subjects; AC, ST, were the project coordinators, and supervised recruitment and analysis; ST conceptualized the present study and methodology. All authors actively contributed to the interpretation of the findings and the development of the final manuscript. All authors have read and agreed to the published version of the manuscript.

Conflict of interest
The authors declare no potential conflict of interest.

Ethics approval and consent to participate
This study received ethical approval from the Ethics Committee of the Provinces of Verona and Rovigo (Ref. CESC15840, 2016). The investigation was conducted in accordance with the latest version of the Declaration of Helsinki (45).

Informed consent
All patients signed a written informed consent before the recruitment.

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Availability of data and materials
The data that support the findings of the article are not publicly available but can be provided by the corresponding author upon reasonable request.

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