Observational study on the QUality of life of Italian Axial SpondyloARthritis patients (QUASAR): baseline data

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Abstract

Objective

To describe the baseline characteristics of the patients enrolled in the QUality of life in patients with Axial SpondyloARthritis (QUASAR) study in terms of quality of life (QoL), disease activity, therapy adherence, and work ability in a real-world setting.

Methods

QUASAR is an Italian multicentre, prospective 12-month observational study, including consecutive adult patients classified as axial spondyloarthritis (axSpA) according to the Assessment of SpondyloArthritis international Society criteria for axSpA.

Results

Of 512 patients enrolled in 23 rheumatology centres, 80.7% had ankylosing spondylitis (AS) and 19.3% had non-radiographic axSpA (nr-axSpA). Mean ages were 34.1±13.3 years at axSpA symptoms onset and 39.5±13.0 years at diagnosis. Of the patients, 51.4% presented with ≥1 extra articular manifestation (EAM); the most common were psoriasis (17.8%) and uveitis (16.4%). Patients with nr-axSpA and AS had similar EAM rates, disease activity, and QoL. Biologic disease-modifying anti-rheumatic drugs (bDMARDs; 83.2%) were the most commonly received medication, followed by conventional synthetic DMARDs (22.9%) and non-steroidal anti-inflammatory drugs (NSAIDs; 16.6%). At baseline, higher treatment satisfaction was reported with bDMARDs which, together with NSAIDs, were associated with the best overall scores for disease activity, function, and QoL in the overall population and AS subgroup.

Conclusion

QUASAR is the first Italian prospective study that comprehensively evaluated a large axSpA patient sample in a real-world setting. This interim analysis at baseline confirmed that i) patients with AS and nr-axSpA have similar QoL and disease burden, ii) nearly all axSpA patients receive treatment, and iii) bDMARDs and NSAIDs, overall, yield better disease activity and QoL.

Key words

ankylosing spondylitis, non-radiographic axial spondyloarthritis, quality of life, epidemiology, Italy

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Introduction

Traditionally, the spondyloarthritis (SpA) group includes ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis (PsA), inflammatory bowel disease-related arthritis, and forms that do not meet established criteria for these defined categories and are labelled as undifferentiated SpA (1).

The concept of axial spondyloarthritis (axSpA) was suggested by the Assessment of SpondyloArthritis international Society (ASAS) a few years ago and has been widely accepted (2). In addition to radiographic axSpA or AS, as defined by the modified New York criteria on the basis of structural damage on pelvis x-rays (3), axSpA also comprises the non-radiographic axSpA (nr-axSpA) form of the disease, in which inflammation of the sacroiliac joints may only be detected by magnetic resonance imaging (MRI) (non radiographic arm). Nr-axSpA also includes patients with a positive test for the presence of the human leucocyte B27 antigen (HLA-B27) and with 2 other SpA features in the absence of imaging evidence of sacroiliac joint involvement (clinical arm).

The relationship between nr-axSpA and AS *(i.e.* whether these are different stages or phenotypes of a unique clinical entity or different diseases) is still being debated (4, 5). Approximately 10% to 20% of patients with nr-axSpA progress to AS within 2 years, whereas about 30% of these patients might never develop the radiographic changes typical of AS over time (6, 7). Risk factors to the progression from nr-axSpA to AS have not been completely identified (6-8).

Tumour necrosis factor-α (TNF-α) inhibitors, which are biologic disease-modifying anti-rheumatic drugs (bDMARDs), have revolutionised the management of patients with axSpA. The scenario of the use of TNF-α blockers for nr-axSpA is multi-faceted: although it is not approved by FDA, the importance of TNF-α blockers in nr-axSpA has been emphasised by the EMA authorisation and, furthermore, it is recommended by both the American College of Rheumatology (ACR), the SpondyloArthritis Research and Treatment Network (SPARTAN) and more recently also by the ASAS/European League Against Rheumatism (EULAR) (9-11). However, real-world data indicate that TNF-α inhibitors are used considerably less frequently in patients with nr-axSpA *versus* those with AS in clinical practice (5). Recently, Sieper and co-workers published an important systematic review evaluating the similarities and differences between nr-axSpA and AS with regard to the treatment effects and clinical, humanistic, and economic burdens (5). Some known dissimilarities between the 2 forms of axSpA were confirmed, including the higher proportion of patients with AS with increased level of C-reactive protein (CRP), and the smaller amount of structural damage and slower radiographic progression in nr-axSpA, while the frequency of HLA-B27 in the 2 forms was found to be similar only in six out of nine studies. Notwithstanding these clinical distinctions, some significant patient-reported outcome (PRO) parameters, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (12), Ankylosing Spondylitis Disease Activity Score (ASDAS) (13), and health-related quality of life (HRQoL) were similar in those with AS and nr-axSpA, suggesting equivalent clinical and humanistic burdens.

At present, observational studies addressing the real-life impact of the burden of axSpA on patient quality of life (QoL), ability to work, costs for healthcare resources for patients and their families exclusively ascribable to the disease and the admission to healthcare assistance, are missing. In an attempt to fill these gaps, the Italian observational QUality of life in patients with Axial SpondyloARthritis (QUASAR) study was undertaken. The primary objective of the study was to assess, in a real-world setting, the evolution of QoL in consecutive patients suffering from the 2 forms of axSpA over a 12-month period, and the impact of the disease on daily activities. This analysis evaluates baseline characteristics of patients enrolled in the QUASAR study in terms of demographics, quality of life (QoL), disease activity, therapy adherence, and work ability in a real-world setting.

Patients and methods

Patient population

Patients were included in the QUASAR study if aged ≥18 years and classified with axSpA according to the ASAS axSpA criteria (2). Exclusion criteria included participation in a clinical study for the treatment of axSpA or a life expectancy of ≤1 year.

The study was approved by each institutional ethics committee/review board (23 approvals; first approval obtained on 18 Feb 2014 by Comitato Etico ASL Lecce, meeting minutes n. 7; no further approval number foreseen by local regulations due to the epidemiological nature of the study) and all patients provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki. The clinical sites were selected on the basis of the availability of an adequate number of subjects affected by axSpA, the utilisation of the ASAS 2009 criteria in routine clinical practice and the availability of an internet connection.

Assessments

In the QUASAR study data were collected, consistently with routine clinical practice, at the study entry (baseline) and after 3, 6, and 12 months.

At each outpatient visit, disease activity was assessed using the ASDAS, BASDAI, Patient's Global Assessment of Disease Activity (PtGA) on a 0- to 100-mm visual analogue scale (VAS), the Physician's Global Assessment of Disease Activity (PGA) on a 0–100 mm VAS, and the presence of dactylitis, enthesitis and axSpA symptoms. At each visit, patients also had to complete the following questionnaires: therapy satisfaction on a VAS, 5-item Medication Adherence Rating Scale (MARS-5) (14), Ankylosing Spondylitis Quality of Life (ASQoL) (15), EuroQoL 5-Dimension 5-Level (EQ-5D-5L) (16), and Work Productivity and Activity Impairment (WPAI) (17). The MARS-5 questionnaire assessed self-reported medication intake behavior using 5 questions rated on a 5-point scale, with a scores ranging from 5 to 25 points. A score of 25 is considered adherent and a score of <25 has been considered to indicate non-adherence. The ASQoL questionnaire measures the impact of axSpA on HRQoL from the patient perspective (15). The questionnaire consists of 18 questions, each with a dichotomous "yes/no" response, scored "1" and "0," respectively. Total scores range from 0 to 18, with higher scores indicating poor HRQoL. The EQ-5D-5L is a generic tool measuring HRQoL and is composed of 2 parts: a descriptive system and a VAS (16). The descriptive system includes 5 single-item dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) to describe the health status of the subject. The VAS evaluates general health on a continuous response scale ranging from 0 (worst possible health state) to 100 (best possible health state). Every dimension of the questionnaire contains 5 answer levels covering no problems (1) to extreme problems (5). Therefore, the descriptive score 11111 represents no problems in all 5 dimensions and a score of 55555 indicates severe/extreme problems in all 5 dimensions. The WPAI questionnaire measures the effect of overall health and specific symptoms on productivity at work and outside work (17). The WPAI-General Health Scale (WPAI-GH) can cover any health problem by indicating the disease/condition of interest in the question. The WPAI-GH consists of 6 items evaluating 4 domains: 1) absenteeism (percentage of working time missed due to health problems in the previous 7 days); 2) presenteeism (percentage of impairment experienced at work due to health problems in the previous 7 days); 3) overall work productivity loss (absenteeism plus presenteeism); and 4) daily activity impairment (percentage of impairment in daily activities due to health problems in the previous 7 days). Higher scores indicate greater work productivity loss and activity impairment.

A web-based electronic case report form was used for data recording.

In case of concomitant administration of medications belonging to different categories, a hierarchical criterion of importance was adopted for the evaluation of disease activity (by BASDAI and ASDAS) and QoL (by ASQoL and EQ-5D-5L) by treatment, as follows: bDMARDs > csDMARDs > NSAIDs. Therefore, a patient receiving a bDMARD plus a csDMARD was included in the bDMARD group, and so on. In contrast, when assessing treatment satisfaction and adherence, each patient was assigned to a specific drug category based on which medication he/she deemed as more relevant.

The present interim analysis includes only the data collected at baseline.

Statistical analysis

The sample size was calculated by assuming a Pearson's correlation coefficient ranging from 0.3 to 0.8 between the total score of the ASQoL questionnaire and the score of Item 6 of the WPAI-GH questionnaire and calculating the relevant confidence interval (CI; 2-way), assuming an alpha error equal to 0.05. A sample of 500 patients enrolled at the baseline visit would have allowed data to be obtained from 392 assessable patients, with a maximal CI of ~0.17, assuming 20% of enrolled patients would not complete the study and 2% would complete the study but have missing data for the total score of the ASQoL questionnaire and/or for the Item 6 score of the WPAI-GH questionnaire.

Quantitative variables were described using mean, standard deviation (SD), median, minimum and maximum values, and qualitative variables were described using absolute and relative frequencies. The Mann-Whitney test, the *t*-test, the χ^2 test, and an analysis of variance were used to calculate differences among subgroups.

Statistical analyses were performed using Stata software v. 12.1 (StataCorp, College Station, TX, USA). Results were considered statistically significant if $p \leq 0.05$.

Results

Patient clinical characteristics

Overall, 512 patients were enrolled in 23 Italian centres from May 2014 to April 2015. Of these patients, 80.7% (n=413) had AS and 19.3% (n=99) nr-axSpA (Table I). Generally, patients with AS were older than patients with nr-axSpA (49.0±12.7 *vs*. 42.5±13.4 years; $p<0.001$) and had a higher male/female ratio (2:1 *vs*. 1:1; $p=0.032$).

Table I. Baseline sociodemographic characteristics of the entire patient population and by the presence of radiographic changes.

Variable	nr-axSpA patients (n=99)	AS patients (n=413)	All patients (n=512)	*p*-value (*)
Age	42.5±13.4	49.0±12.7	47.8±13.1	**<0.001**
Males/females	53/46 (53.5/46.5)	265/148 (64.2/35.8)	318/194 (62.1/37.9)	**0.032**
Civil status				
Single	35 (36.4)	79 (19.1)	114 (22.3)	**0.001**
Married	57 (57.6)	305 (73.8)	362 (70.7)	
Widower	0 (0.0)	11 (2.7)	11 (2.1)	
Divorced	7 (7.1)	18 (4.4)	25 (4.9)	
Living				
Alone	11 (11.1)	36 (8.7)	47 (9.2)	0.643
With family	88 (88.9)	374 (90.6)	462 (90.2)	
Other	0 (0.0)	3 (0.7)	3 (0.6)	
Education				
Primary school	4 (4.0)	31 (7.5)	35 (6.8)	0.125
Secondary school	24 (23.2)	128 (31.0)	152 (29.7)	
High school	53 (53.5)	208 (50.4)	261 (51)	
Degree	16 (16.2)	44 (10.7)	60 (11.7)	
PhD	2 (2.0)	2 (0.5)	4 (0.8)	
Working status				
Employed	62 (62.6)	247 (59.8)	309 (60.4)	**0.042**
Student	8 (8.1)	13 (3.1)	21 (4.1)	
Housekeeper	11 (11.1)	41 (9.9)	52 (10.2)	
Retired	7 (7.1)	66 (16.0)	73 (14.3)	
Unemployed	11 (11.1)	46 (11.1)	57 (11.1)	
Smoking status				
Never smoker	56 (56.6)	212 (51.3)	268 (52.3)	0.472
Smoker	20 (20.6)	105 (25.4)	125 (24.4)	
Ex-smoker (≥6 months)	23 (23.2)	96 (23.2)	119 (23.2)	
Health system exemption	88 (88.9)	396 (95.7)	484 (94.5)	**0.049**
Needing caregivers	6 (6.1)	25 (6.1)	31 (6.1)	0.952
Needing auxiliary aids	1 (1.0)	7 (1.7)	8 (1.6)	1.000

Data are reported as mean ± standard deviation or frequencies (n [%]).
(*) *p*-value refers to the comparison between the non-radiographic and radiographic axSpA subgroups. AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; nr-axSpA, non-radiographic axial spondyloarthritis.

Among the 512 enrolled patients, a significant difference was observed with regard to civil status, working status, and national health system co-payment waiver, with the latter being more common among patients with AS (95.7% *vs*. 88.9%, *p*=0.049).

Table II shows the clinical characteristics at baseline. Overall, the mean age at axSpA onset was 34.1±13.3 years and was 39.5±13.0 years at diagnosis; the mean time from disease onset to diagnosis was 5.4±7.2 years. The time to diagnosis was shorter in patients with nr-axSpA than in patients with AS (3.8±5.7 *vs*. 5.8±7.4; *p*=0.008). Of the 512 patients, 97 (18.9%) had had familiarity for SpA and 108 (21.1%) for psoriasis. Of the patients with available HLA typing, 60.9% (249/409) were positive for the presence of HLA-B27; with no significant differences between nr-axSpA and AS. At the first study visit, the mean CRP level was 0.8±2.2 mg/dL (normal <0.5 mg/dL). As far as axial pain was concerned, 73.3% (220/300) had low back pain, 35.3% (106/300) had cervical pain, and 23.3% (70/300) had dorsal pain. In terms of peripheral manifestations, 14.1% of patients (72/512) had enthesitis and 0.6% (3/512) had dactylitis. Regarding extra-articular manifestations (EAMs; past or present at baseline), overall, 51.4% of patients (263/512) presented with ≥1 EAM, with a similar frequency between nr-axSpa (55.7% [54/97]) and AS (50.4% [209/415]. The most common EAMs were psoriasis (17.8%; 91/512), uveitis (16.4%; 84/512), Crohn's disease (6.8%; 35/512), and ulcerative colitis (4.5%; 23/512).

Treatment

Overall, 96.9% of patients (496/512; 96 patients with nr-axSpA and 400 patients with AS) were undergoing treatment at the time of the first visit. A summary of medications administered is reported in Table III. The drugs administered most frequently included bDMARDs (83.2%; n=426), including adalimumab, etanercept, infliximaband golimumab, followed by conventional synthetic DMARDs (csDMARDs; 22.9%; n=117, mainly methotrexate and sulfasalazine) and non-steroidal anti-inflammatory drugs (NSAIDs; 16.6%; n=85). The proportion of patients receiving bDMARDs was higher in the AS (85.0%) than in the nr-axSpA group (75.8%). More patients with nr-axSpA than with AS received NSAIDs (24.2% [24/99] *vs*. 14.8% [61/413], respectively), whereas the rate of treatment with csDMARDs was similar (25.3% [25/99] *vs*. 22.3% [92/413, respectively]). Among patients with nr-axSpA, the most frequently administered agents were adalimumab (47.5%; n=47), etanercept (19.2%; n=19), and methotrexate (18.2%; n=18), whereas among patients with AS, 32.0% (n=132) received adalimumab, 21.3% (n=88) received infliximab, 18.2% (n=75) received etanercept, and 12.3% (n=51) received golimumab.

Disease activity and Quality of Life Scores

Data on the scores of disease activity (PGA and PtGA, BASDAI, and ASDAS), QoL (ASQoL and EQ-5D-5L VAS), and work ability (WPAI) were obtained from >97% of patients at baseline. As shown in Table II, no significant difference was observed in terms of disease activity, QoL, and WPAI between patients with AS and nr-axSpA. BASDAI and ASDAS mean values were respectively 3.2±2.5 and 2.1±1.1, indicating an overall mild disease activity. The impact on QoL was nevertheless considerable, since ASQoL reached an overall score of 5.8±5.5 and EQ-5D VAS was 66.3±21.8; activity impairment was 34.8%±28.6.

Figures 1 and 2 show the mean values of the scores related to disease activity (BASDAI and ASDAS), work ability

Table II. Baseline clinical characteristics of the entire patient population and by the presence of radiographic changes.

Variable	nr-axSpA patients (n=99)	AS patients (n=413)	All patients (n=512)	*p*-value (*)
Age at onset, years	34.1 ± 14.1	34.1 ± 13.2	34.1 ± 13.3	0.789
Age at diagnosis, years	37.8 ± 13.0	39.94 ± 13.0	39.5 ± 13.0	0.106
Time to diagnosis, years	3.8 ± 5.7	5.8 ± 7.4	5.4 ± 7.2	**0.008**
Time from onset, years	8.4 ± 8.2	14.9 ± 10.3	13.7 ± 10.3	**<0.001**
Time from diagnosis, years	4.7 ± 5.3	9.1 ± 7.5	8.3 ± 7.3	**<0.001**
SpA familiarity	14 (14.1)	83 (20.1)	97 (18.9)	0.215
Psoriasis familiarity	25 (25.3)	83 (20.1)	108 (21.1)	0.215
HLA-B27				
Positive	40/73 (54.8)	209/336 (62.2)	249/409 (60.9)	0.273
CRP, mg/dL	0.7 ± 1.3	0.8 ± 2.4	0.8 ± 2.2	0.669
Axial pain	61 (61.6)	239 (57.9)	300 (58.6)	0.789
Low back	51 (83.6)	169 (70.7)	220 (73.3)	0.150
Cervical	15 (24.6)	91 (38.1)	106 (35.3)	0.090
Dorsal	14 (23.0)	56 (23.4)	70 (23.3)	0.679
Peripheral manifestations				
Enthesitis	14 (14.4)	58 (14.0)	72 (14.1)	0.872
Dactylitis	1 (1.0)	2 (0.5)	3 (0.6)	0.519
Extra-articular manifestations	54 (55.7)	209 (50.4)	263 (51.4)	0.5
Psoriasis	24 (24.2)	67 (16.2)	91 (17.8)	0.08
Uveitis	16 (16.2)	68 (16.5)	84 (16.4)	1.00
Crohn's disease	4 (4.0)	31 (7.5)	35 (6.8)	0.27
Ulcerative colitis	5 (5.0)	18 (4.4)	23 (4.5)	0.78
Comorbidities	39 (40.2)	174 (41.9)	213 (41.6)	0.65
Hypertension	8 (8.1)	74 (17.9)	82 (16.0)	**0.023**
Allergies	10 (10.1)	21 (5.1)	31 (6.1)	0.111
Anxiety/depression	4 (4.0)	14 (4.4)	22 (4.3)	0.791
Physician's global assessment	2.8 ± 2.5	2.7 ± 2.7	2.8 ± 2.7	0.627
Patient's global assessment	4.0 ± 2.6	3.6 ± 2.8	3.6 ± 2.7	0.545
BASDAI	3.6 ± 2.5	3.1 ± 2.4	3.2 ± 2.5	0.861
ASDAS	2.2 ± 1.1	2.1 ± 1.1	2.1 ± 1.1	0.468
ASQoL	6.2 ± 5.6	5.7 ± 5.4	5.8 ± 5.5	0.429
EQ-5D-5L (VAS)	63.3 ± 23.5	67.0 ± 21.3	66.3 ± 21.8	0.926
WPAI	37.6 ± 29.4	34.2 ± 28.4	34.8 ± 28.6	0.115

Data are reported as mean ± standard deviation or frequencies (n [%]).
*p-value refers to the comparison between the non-radiographic and radiographic axSpA subgroups.
AS: ankylosing spondylitis; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASQoL: Ankylosing Spondylitis Quality of Life; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; EQ-5D-5L: EuroQoL 5-Dimension 5-Level; HLA-B27: human leukocyte antigen B27; nr-axSpA: non-radiographic axial spondyloarthritis; SpA: spondyloarthritis; VAS: visual analogue scale; WPAI: Work Productivity and Activity Impairment.

Table III. Therapies given, at baseline, to the entire population and by radiographic involvement.

Drugs	nr-axSpA patients (n=99)	AS patients (n=413)	All patients (n=512)
bDMARDs	75 (75.8)	351 (85.0)	426 (83.2)
csDMARDs	25 (25.3)	92 (22.3)	117 (22.9)
NSAIDs	24 (24.2)	61 (14.8)	85 (16.6)
Corticosteroids	6 (6.0)	21 (5.1)	27 (5.3)
Analgesics	1 (1.0)	17 (4.1)	18 (3.5)
Other	4 (4.0)	26 (6.3)	30 (5.9)

Data are reported as frequencies (n [%]).
Therapies were given to 496 of 512 patients (96.9%) overall, 96 of 99 of patients with nr-axSpA (97.0%) and 400 of 413 of patients with AS (96.9%).
AS: ankylosing spondylitis; bDMARD: biologic disease-modifying anti-rheumatic drug; csDMARD: conventional synthetic disease-modifying anti-rheumatic drug; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug.

(WPAI), and QoL (ASQoL, EQ-5D-5L) by treatment class, both in the entire population and in the nr-axSpA and AS subgroups. Disease activity was significantly lower in patients receiving bDMARDs and NSAIDs versus csDMARDs (Fig. 1A-B), in both the overall population and AS subgroup, but not among patients with nr-ax-SpA, which was likely due to the small sample size. A trend toward better work ability was observed in patients treated with bDMARDs and NSAIDs, *versus* csDMARDs in all 3 groups (Fig. 1C). Finally, both ASQoL and EQ-5D-5L indicated a better QoL in the whole population and patients with AS receiving bDMARDs and NSAIDs versus csDMARDs, although significance was reached only in the case of the EQ-5D-5L. A trend toward better EQ-5D-5L scores was also observed among patients with nr-axSpA (Fig. 2A-B).

The mean score indicating patient satisfaction with therapy was 73.2±30.2. When the satisfaction with treatment was assessed by treatment class, a trend toward higher scores was reported among patients treated with bDMARDs compared with csDMARDs and NSAIDs (Fig. 3A) in both subgroups. The mean MARS-5 score, indicating adherence to treatment, was 23.8±2.3 in the entire population. It was significantly higher in patients receiving bDMARDS and csDMARDs compared with NSAIDs in both the entire population and the AS subgroup, whereas in patients with nr-axSpA, the difference did not reach significance, likely due to the limited sample size (Fig. 3B). For both satisfaction and adherence, no difference was observed between the diagnostic subgroups.

Discussion

The main aim of the QUASAR study was to assess, over a 12-month period, the QoL of patients with AS and nr-axSpA in a real-world setting. Of the 512 consecutive patients meeting the ASAS classification criteria for axSpA and recruited in 23 Italian rheumatology centers, 19.3% had nr-axSpA and 80.7% had AS.

The population in our study is older than in other reports (average age being 49.0

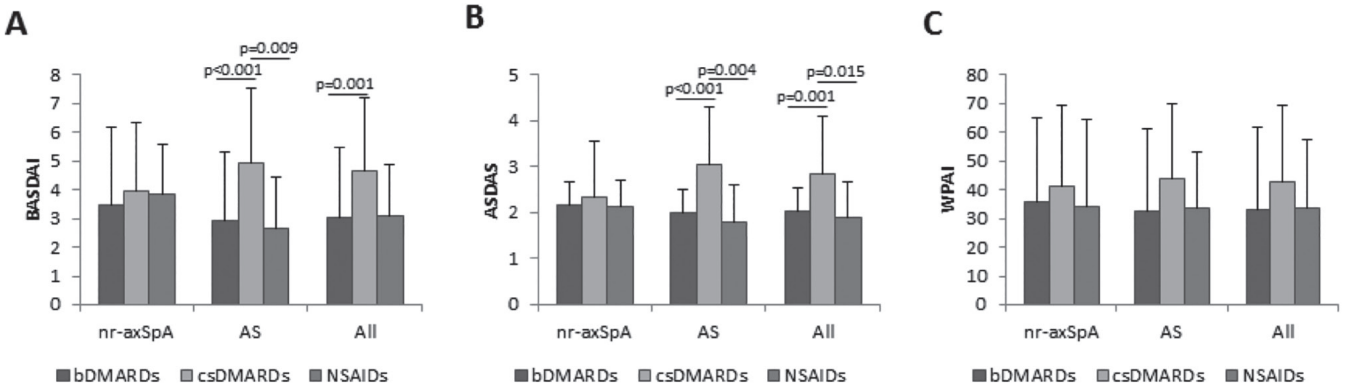

Fig. 1. Mean (± standard deviation) scores related to disease activity (**A**, **B**) and work ability (**C**) by treatment class in the entire population and by disease subgroups.
AS: ankylosing spondylitis; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biologic disease-modifying anti-rheumatic drug; csDMARD: conventional synthetic disease-modifying anti-rheumatic drug; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug; WPAI: Work Productivity and Activity Impairment.

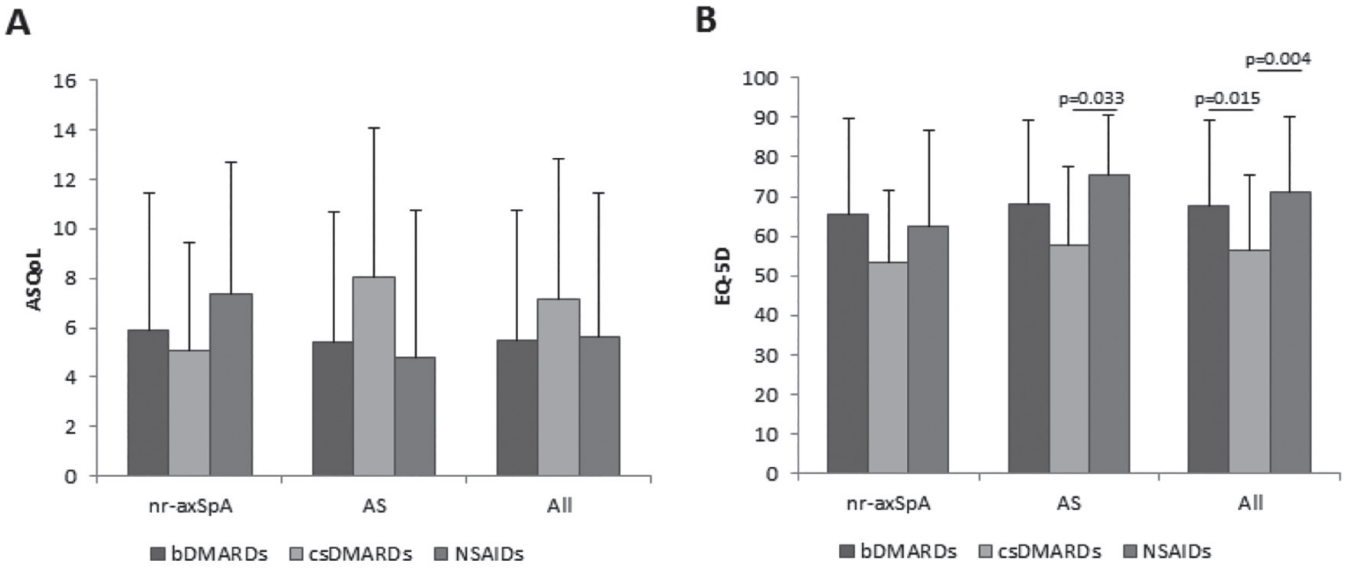

Fig. 2. Mean (± standard deviation) scores related to quality of life (**A**, **B**) by treatment class in the entire population and by disease subgroups.
AS: ankylosing spondylitis; ASQoL: Ankylosing Spondylitis Quality of Life; bDMARD: biologic disease-modifying anti-rheumatic drug; csDMARD: conventional synthetic disease-modifying anti-rheumatic drug; EQ-5D-5L: EuroQoL 5-Dimension 5-Level; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug.

and 42.5 years, in AS and nr-axSpA patients respectively), and also the mean age at the axSpA onset (34.1 years) was older. While the older age at onset might derive from a recall bias because the data was either anamnestic or reported by the patient, the older average age at baselinet might be due to the consecutive enrolment design: our population represents a sample of the axSpa population that was visited at different Italian centres in their clinical routine in the period when the study was conducted.

As a consequence of the recruitment process that did not exclude patients already on medication, nearly all patients (496/512) were receiving treatment at baseline, with TNF-α blockers being the most frequently prescribed regimens.

Patient QoL was measured using the ASQoL and the EQ-5D-5L questionnaires. Both instruments documented a similar level of QoL in both groups. Mean ASQoL levels were 6.2±5.5 in patients with nr-axSpA and 5.7±5.4 in patients with AS (p=0.429). In the Herne cohort, which included 100 consecutive patients who were not treated with bDMARDs, the values were 4 *versus* 5.5 (18). EQ-5D-5L VAS mean values in our study were 63.3±23.5 in patients with nr-axSpA and 67.0±21.3 in patients with AS (p=0.926). In the Swiss Clinical Management study, an observational cohort study on patients meeting the axial ASAS classification criteria, baseline EQ-5D-5L VAS scores were 66.4 in patients with nr-axSpA and 68.8 in patients with AS (p=0.13) (19). Our data confirm that the 2 forms of axSpA, AS and nr-axSpA, present a similar burden in terms of disease activity, physical function, and QoL.

Patients were stratified according to disease subtype, therapy administered, and scores analysed. A trend toward higher treatment satisfaction with bDMARDs and higher adherence to treatment with bDMARDs and csDMARDs versus NSAIDs was observed, the latter being

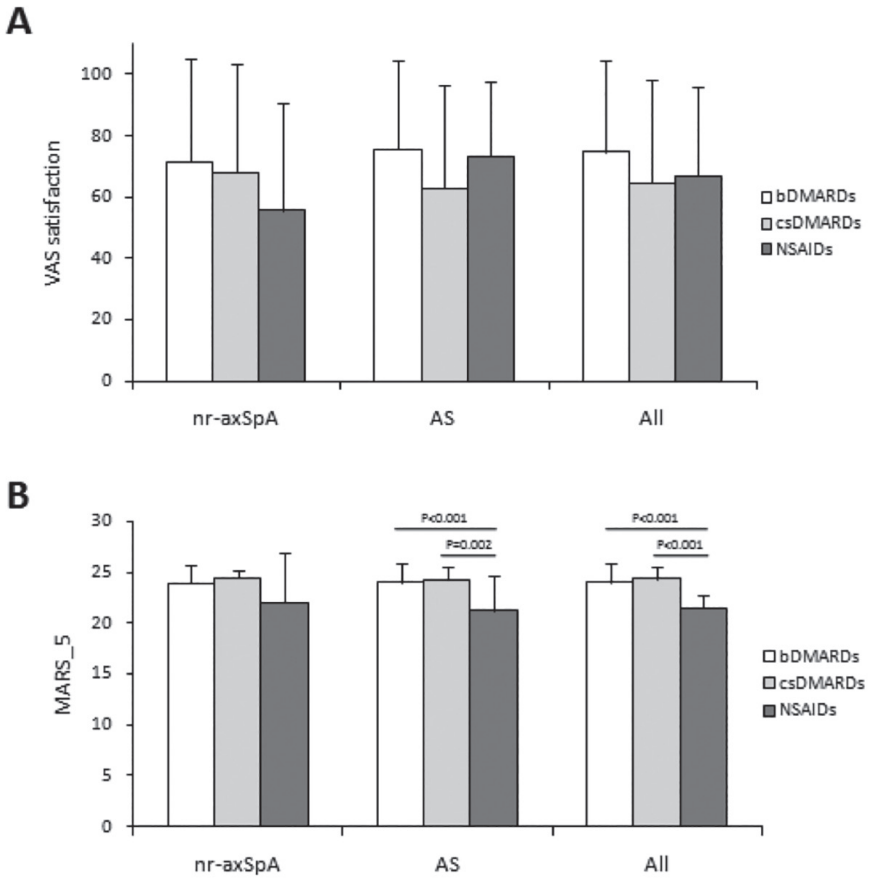

Fig. 3. Mean (± standard deviation) VAS satisfaction (**A**) and MARS-5 (**B**) scores by treatment class in the entire population and by disease subgroup.
AS: ankylosing spondylitis; bDMARD: biologic disease-modifying anti-rheumatic drug; csDMARD: conventional synthetic disease-modifying anti-rheumatic drug; MARS-5: Medication Adherence Report Scale-5; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug; VAS: visual analogue scale.

the recommended agents for first-line treatment, regardless of radiographic changes. Similarly, of all indices related to disease activity, function, QoL and activity impairment in the overall population and the AS subgroup, patients treated with biologics and NSAIDs had the best overall scores. The lower disease activity indexes found in the bDMARDs treated group are likely due to the effect of the treatment, that was already ongoing at the time of the visit, being the study observational.

In our study, the patients with nr-axSpA were younger, had a shorter disease duration, and were more frequently women than patients with AS, which is in line with other published series of patients with axSpA (6).

In the QUASAR study, the prevalence of EAMs was analysed and the results indicated that psoriasis and uveitis were the most frequent EAMs, followed by Crohn's disease and ulcerative colitis, with similar rates in the 2 subtypes. Two recent meta-analyses have addressed the prevalence of EAMs in patients with AS and in patients with AS versus nr-axSpA (20, 21). Both reported that the most prevalent EAM was uveitis, with a pooled prevalence of 25.8% in the first study and 23.0% in AS and 15.9% in nr-axSpA in the second study (20, 21), whereas the pooled prevalence of psoriasis was 9.3% in the first study and 10.2% in AS and 10.9% in nr-axSpA in the second one. The prevalence of inflammatory bowel disease was 6.8% in AS in the first study and 4.1% in AS and 6.4% in nr-axSpA in the second study.

QUASAR was the first observational prospective study conducted in a large population of axSpA patients, representative of patients with AS and nr-axSpA in Italy, that comprehensively assessed QoL, its modifications over time, and the correlation to social aspects, by collecting a wide spectrum of information. We acknowledge that a limitation of this study is mainly due to its purely observational design, therefore patients were already treated according to clinical practice by different amounts of time, making it more difficult to interpret the results. Another limitation is that patient's functional assessment was not performed, making it impossible to evaluate this aspect and the correlation with disease activity and QoL or assessing similarities and differences between AS and nr-axSpa.

Our study showed similar burden of disease between AS and nr-axSpa patients in terms of disease activity, QoL and work ability impairment, and considering that WPAI could be influenced by both disease activity and patient's functional assessment, we can assume that physical impairment between the two clinical entities could be similar, but in in the absence of a specific assessment this assumption remains unproven in our population.

In conclusion, the baseline data of the QUASAR study showed that QoL is similarly reduced in patients with nr-axial SpA and AS. Moreover, our data showed that, in clinical practice, Italian rheumatologists treat nearly all patients with nr-axSpA and frequently use bDMARDs. Notably, bDMARD and NSAID use was associated with lower disease activity and better QoL. It will be valuable to evaluate the modifications of QoL over the 12-month follow-up period and determine the economic burden of these 2 forms of axSpA.

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