Is the impact of biologic agents in enteropathic spondylitis different from other spondylitis? Real life data from the HUR-BIO Registry

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Abstract

Objective

To compare enteropathic spondylitis (ES) with psoriatic spondylitis (PS) and ankylosing spondylitis (AS), in patients on biological disease-modifying anti-rheumatic drug (bDMARD) treatment.

Method

Patients who were enrolled in the HUR-BIO registry were included. ES patients were considered as the main study group; AS and PS patients were included as the control groups. ES was defined as patients with inflammatory bowel disease (IBD) having inflammatory back pain/spine symptoms plus radiological sacroiliitis.

Results

Sixty-four ES patients (46.9% female), 128 AS patients (39.1% female), and 92 PS patients (62% female) were analysed. Baseline erythrocyte sedimentation rate (ESR) was significantly higher in the ES group than in the AS group. Both the baseline ESR and C-reactive protein were also higher in the ES group compared with the PS group. Among the first bDMARD use, infliximab use was higher in the ES group than the other groups. There was a marginal significant difference between the SpA subgroups in the retention rates of the first bDMARDs (log-rank, p=0.059). Ulcerative colitis was a significant predictor for switching of bDMARDs in comparison to Crohn's disease. Regarding the treatment responses, no significant differences were relevant for the three groups in terms of 50% improvement of the initial Bath Ankylosing Spondylitis Disease Activity Index score, the Assessment of Spondyloarthritis International Society partial remission score, and 20% improvement of ASAS score.

Conclusion

A large majority of enteropathic spondyloarthritis patients on bDMARD treatment had radiographic sacroiliitis. ES patients had distinctive features that distinguish them from AS and PS patients.

Key words

enteropathic spondyloarthritis, spondylitis, inflammatory bowel disease, real-life, retention rate

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Introduction

Spondyloarthritis (SpA) is a group of disorders that share common clinical features and pathogenic pathways. Enteropathic spondyloarthritis (eSpA) is one of the diseases in the SpA spectrum in which axial and/or peripheral joint involvement, enthesitis, and dactylitis are accompanied by Crohn's disease (CD) or ulcerative colitis (UC) (1, 2). According to the dominant joints that are involved, eSpA can be classified into two main categories as peripheral and axial enteropathic arthritis. Moreover, another type has been described, which includes patients with both axial and peripheral forms (3, 4).

Axial involvement which may be associated with the chronic IBD course (5), can be in the form of ankylosing spondylitis (AS) (according to the modified New York (mNY) criteria; bilateral at least grade 2 or unilateral at least grade 3 sacroiliitis) or in the form of non-radiographic axial spondyloarthropathy (nr-axSpA). There are similarities and differences in clinical and radiological features of axial involvement among eSpA, AS, and psoriatic arthritis (PsA). The clinical and radiological course of axial involvement in eSpA is similar to AS but radiologically may differ from PsA and the disease progression causes an increase in spine immobility, which results in ankylosis (2, 6, 7).

In this study, of the 2.507 SpA patients on bDMARD treatment, 90 were eSpA, and 64 of those 90 had sacroiliitis and were named enteropathic spondylitis (ES). Of the 469 PsA patients, 92 had sacroiliitis and were named PS. Also, 128 AS patients, age- and disease duration-matched with ES, were selected. The primary objective of the current study was to compare ES patients with PS and AS patients, in terms of demographic, clinical, laboratory, outcome measures. Secondary objectives were to determine treatment response and retention rates of bDMARDs in these SpA subgroups.

Materials and methods

Study population and selection of control group

The present study included patients who were enrolled in the Hacettepe University Rheumatology Biologic Registry (HUR-BIO). The HUR-BIO is a single and independent data recording system of bDMARD treatment, which was established in 2005 and has been prospective since 2012 (8). Until January 2019, there were 2.507 SpA patients in the HUR-BIO registry. All patients were on bDMARD treatment including anti-tumour necrosis factor (anti-TNF) treatments or anti-IL-17 treatment. Overall, 1.842 (73.5%) patients were classified as AS according to the mNY criteria, 106 (4.2%) patients had nr-axSpA, 469 (18.7%) patients had PsA, and 90 (3.6%) patients had eSpA. eSpA was defined as axial and/or peripheral joint involvement with IBD and 64 (71%) of 90 eSpA patients had radiological sacroiliitis according to the mNY criteria. ES was defined as patients with IBD (UC or CD) having inflammatory back pain/spine symptoms plus radiographic sacroiliitis according to the mNY criteria. Patients with ES (n=64) were selected as the main study group and age- and disease duration-matched 128 AS patients were selected as the control group. Moreover, 92 (19.6%) of 469 PsA patients had sacroiliitis according to the mNY criteria, which named as PS, and all PS patients were also enrolled as the control group.

Data collection and outcome measures

Data on demographic, clinical, and laboratory features including age, sex, disease duration, age at disease onset, age at IBD onset, family history of SpA, history of uveitis, peripheral involvement (ever) and HLA-B27 (if available) were collected. Outcome measures were Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score, Bath Ankylosing Spondylitis Functional Index (BASFI) score, Visual Analogue Scale-patient global assessment (PGA-VAS; 0–100 mm) score, pain-VAS (0–100 mm) score, fatigue-VAS (0–100 mm) score, morning stiffness duration (minutes), erythrocyte sedimentation rate (ESR; mm/h), and C-reactive protein (CRP; mg/L) level. These outcome measure parameters routinely recorded as a part of clinical assessment of patients. All patients had

conventional sacroiliac and/or pelvic x-ray images, which were re-assessed by an experienced rheumatologist (UK) for grading of sacroiliitis. In addition, syndesmophytes were evaluated by the same experienced rheumatologist (UK) and conventional lumbar and/or cervical radiographs were available in 75%, 83%, and 54% of the patients with ES, AS, and PS, respectively.

Initial bDMARDs such as anti-TNF drugs (adalimumab, certolizumab pegol, etanercept, infliximab, and golimumab) and anti-IL-17 (secukinumab) and concomitant conventional DMARDs (cDMARD; sulphasalazine and methotrexate) were recorded. During the follow-up period, use of bDMARDs, switching of bDMARDs (if yes, reasons of change), and response to bDMARDs were assessed every single outpatient visit. Response to bDMARDs was defined as a 50% improvement of the initial BASDAI scores (BASDAI 50) after both first and last visits. Treatment response to bDMARD was also evaluated by the Assessment of Spondyloarthritis International Society (ASAS) scores; ASAS partial remission (PR) score and a 20% improvement of ASAS scores (ASAS 20). Both ASAS PR and ASAS 20 include four domains: patient global assessment of disease activity, pain, function (assessed by BASFI), and inflammation (a mean of the BASDAI questions 5 and 6) (9). ASAS PR was defined as a value ≤2 for each of the domains on a scale of 10. ASAS 20 improvement was defined as at least 20% and at least one unit improvement in at least three of the four areas on a 0-10 scale; no worsening of more than 20% and more than 1 unit in the remaining area should be observed (10).

Our study is compatible with the Declaration of Helsinki and was approved by the ethics committee of Hacettepe University (approval no.: KA17 / 058).

Statistical analysis

Data was analysed using the Statistical Package for the Social Sciences for Windows, v. 22.0 (IBM Corp., Armonk, NY, USA). The variables were investigated using visual (histogram and probability plots) and analytical methods (Kolmogorov-Smirnov, skewness, and kurtosis) to determine whether they were normally distributed. Normally distributed variables were expressed as mean and standard deviation (SD) and non-normally distributed variables were expressed as median and interquartile range (IQR). Categorical variables were presented as absolute frequencies and percentages. Categorical variables were compared using the Chi-squared test or Fisher's exact test, when appropriate. The Student t-test and the Mann-Whitney U-test were used to compare the normally- and non-normally distributed continuous variables, respectively, between two groups.

Retention rates of bDMARDs were assessed by the Kaplan-Meier survival analysis for all three diseases according to a change in the first bDMARD. The differences between survival curves were determined by the log-rank test. The possible factors identified by univariate analyses were further entered into the Cox regression analysis, with backward selection, to determine independent predictors of survival. Among correlated factors with similar effects on survival, only those with clinical significance were included. A 5% type-I error level was used to infer statistical significance.

Results

Comparison of ES patients with AS and PS patients

Sixty-four eSpA patients (46.9% females), who had sacroiliitis, were enrolled into the final analysis as the main study group. Their mean age was 45.0±12.0 years and mean disease duration was 9.2±6.9 years. IBD type was UC in 34 (53.1%) patients and CD in 30 (46.9%) patients. As the control groups, 128 AS patients and 92 PS patients were included in the analysis. Comparisons of demographic and clinical characteristics of these 3 groups are presented in Table I. According to the comparison between ES and AS groups, the rate of concomitant cDMARD use (35.9% *vs.* 10.2%, $p<0.001$) and the baseline ESR value (33.5 [39.7] mm/h *vs.* 22 [33.7] mm/h, $p=0.03$) were significantly higher in the ES group. On the other hand, the rate of uveitis history (6.3% *vs.* 21.8%, $p<0.001$) and the duration of bDMARD use (51 [71.3] months *vs.* 69.8 [38.9] months, $p=0.006$) were significantly higher in the AS group. Moreover, the baseline level of acute phase reactants (both ESR and CRP) and concomitant sulphasalazine use were significantly higher in the ES group than those in the PS group. In addition, concomitant methotrexate use and family history of SpA were significantly higher in the PS group than those in the ES group. The baseline disease activity scores and functional statuses were found similar in all SpA subgroups. Also, concomitant peripheral arthritis (ever) was similar in all SpA subgroups.

When the ES patients were separately analysed according to the IBD subgroups (CD and UC), family history of SpA was more common in the CD group than in the UC group (36.7% *vs.* 14.7%, $p=0.04$). In addition, HLAB-27 positivity was similar in the CD and UC patients (53.8% *vs.* 28.6%, $p=0.1$).

Choice of bDMARD and rate of switching in the SpA subgroups

ES, AS, and PS patients were on bDMARD treatment for 51.0 (IQR 71.3), 69.8 (IQR 38.9), and 54.1 (IQR 80.7) months, respectively. During these periods, bDMARD switching rates were 50%, 35.9%, and 42.4% in the ES, AS, and PS groups, respectively ($p=0.17$). The first and last bDMARDs used by the patients are shown in Figure 1. Among the first bDMARDs used by the groups, infliximab treatment was significantly higher in the ES group than both in the AS group (41% *vs.* 19%, *vs.* $p=0.002$) and PS group (41% *vs.* 19%, $p=0.001$).

In the ES group, switching rate between bDMARDs was 50.0% (66.7% in the CD patients and 35.3% in the UC patients, $p=0.01$) during the follow-up period and the reasons for switching were as follows: ineffectiveness in 19 (30%) patients, side effects in 6 (9%) patients, and other events (such as patient's own willingness, inability to reach a doctor, and unknown reasons) in 7 (11%) patients. The rate of patients using etanercept in the ES group decreased from 14% to 2% during the follow-up.

Table I. Demographic features and outcome measures in the spondyloarthritis subgroups on bDMARD treatment.

	ES n=64	AS n=128	PS n=92	*p*1	*p*2
Female, n (%)	30 (46.9)	50 (39.1)	57 (62.0)	0.35	0.07
Age, years, mean ± SD	45.0 ± 12.0	45.3 ± 10.6	41.8 ± 12.2	0.69	0.21
Age at diagnosis, years, mean ± SD	35.6 ± 11.0	34.8 ± 10.5	34.1 ± 11.6	0.99	0.83
Disease duration, years, mean ± SD	9.2 ± 6.9	10.5 ± 5.4	7.7 ± 6.9	0.12	0.19
HLA-B27, positive/total (%)	11/27 (40.7)	31/52 (59.6)	13/33 (39.4)	0.11	0.91
Family history of SpA, n (%)	16 (25.0)	25 (19.5)	37 (40.2)	0.38	**0.048***
Uveitis, n (%)	4 (6.3)	28 (21.8)	2 (2.2)	**<0.001***	0.19
Peripheral arthritis (ever), positive/total (%)	25/61 (41)	35/128 (27.3)	41/90 (45.6)	0.06	0.58
Syndesmophyte, positive/total (%)	21/48 (43.8)	45/106 (42.5)	15/50 (30)	0.88	0.16
Smoking (current smoker or ex-smoker), n (%)	37 (57.8)	79 (61.7)	49 (53.3)	0.602	0.57
Duration of bDMARD use, months, median (IQR)	51.0 (71.3)	69.8 (38.9)	54.1 (80.7)	**0.006***	0.82
Switching between bDMARDs, n (%)	32 (50.0)	46 (35.9)	39 (42.4)	0.09	0.24
At least one concomitant cDMARD use, n (%)	23 (35.9)	13 (10.2)	47 (51.1)	**<0.001***	0.06
Methotrexate	7 (10.9)	5 (3.9)	25 (27.2)	0.109	**0.013***
Sulphasalazine	15 (23.4)	9 (7.0)	8 (8.7)	**0.001***	**0.01***
BASDAI score, mean ± SD	5.7 ± 2.1	5.4 ± 1.7	5.8 ± 1.8	0.19	0.85
BASFI score, median (IQR)	4.6 (5.7)	3.5 (3.7)	4.1 (4)	0.32	0.39
ESR, mm/h, median (IQR)	33.5 (39.7)	22 (33.7)	18 (27.5)	**0.03***	**<0.01***
CRP, mg/dL, median (IQR)	1.6 (4.1)	1.3 (2.2)	1.05 (1.9)	0.21	**0.01***
PGA-VAS, median (IQR)	60 (27.5)	50 (30)	60 (30)	0.12	0.73
Pain-VAS, median (IQR)	70 (30)	60 (40)	70 (30)	0.21	0.54
Fatigue-VAS, median (IQR)	70 (20)	50 (30)	70 (30)	0.09	0.58
Morning stiffness, minutes, median (IQR)	48 (69)	60 (67.8)	60 (100)	0.67	0.47

*p<0.05; p1: p-value between ES and AS; p2: p-value between ES and PS
Among the ES, AS, and PS groups, PGA-VAS score was available in 44, 91, and 61 patients, respectively; pain-VAS score was available in 36, 78, and 53 patients, respectively; fatigue-VAS score was available in 36, 75, and 49 patients, respectively; and morning stiffness duration was available in 34, 75, and 47, patients, respectively.
ES: Enteropathic spondylitis; AS: Ankylosing spondylitis; PS: Psoriatic spondylitis; SpA: Spondyloarthritis; bDMARD: Biological disease-modifying antirheumatic drug; cDMARD: conventional disease-modifying anti-rheumatic drug; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PGA-VAS: Visual Analogue Scale - patient global assessment; SD: standard deviation; IQR: inter-quartile range

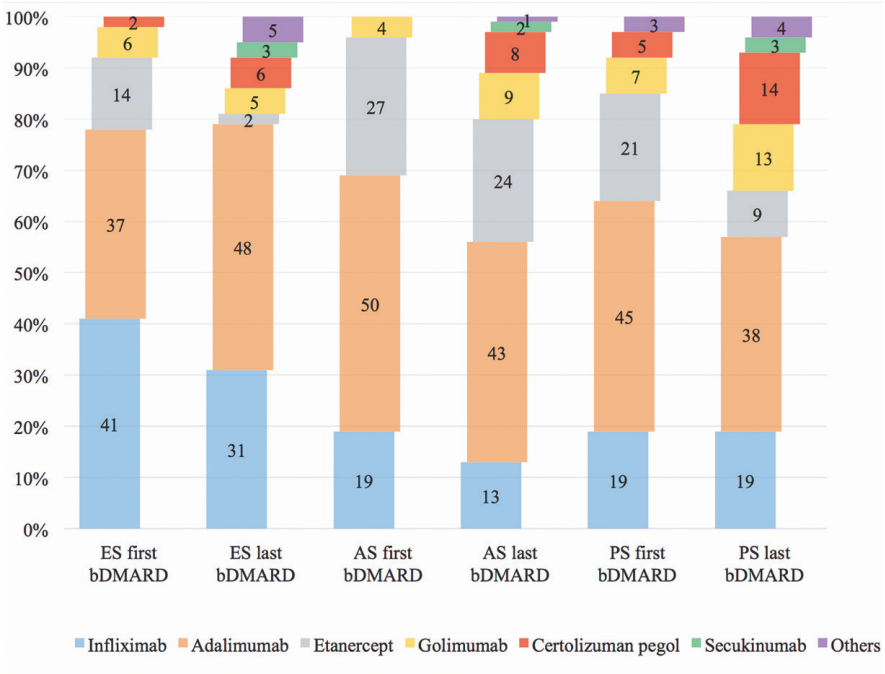

Fig. 1. Distribution of the first and last bDMARDs in the study groups
For infliximab, p=0.002 between the ES and AS groups and p=0.001 between the ES and PS groups. There were no differences between the groups in terms of other bDMARDs.
bDMARD: biological disease-modifying anti-rheumatic drug; ES: enteropathic spondylitis; AS: ankylosing spondylitis; PS: psoriatic spondylitis.

Treatment response and retention rates of bDMARDs in the SpA subgroups

The first outpatient control visit was after 6.4 (IQR 30.1) months in 57 of 64 ES patients, after 5.9 (IQR 25) months in 120 of 128 AS patients, and after 9.7 (IQR 46.4) months in 79 of 92 PS patients (p=0.46). Regarding the response to bDMARD treatments, there were no significant differences between the SpA groups in terms of BASDAI 50 improvement, ASAS PR, and ASAS 20 improvement both at the first and last control visits (Table II). When the treatment response to bDMARD was evaluated according to the IBD subgroups, the BASDAI 50 improvement at the last visit was significantly higher in the CD group than in the UC group (50% *vs.* 19%, p=0.028). However, there were no significant differences between the CD and UC groups regarding the BASDAI 50 improvement at the first visit and regarding the ASAS PR and ASAS 20 improvement both at the first and last visits.

Table II. Follow-up period and response to bDMARD treatment in all spondyloarthritis subgroups.

	ES		AS		PS		p3	p4
	First visit	Last visit	First visit	Last visit	First visit	Last visit		
Control visit months, median (IQR)	6.4 (30.1)	51 (71.3)	5.9 (25)	69.8 (38.9)	9.7 (46.4)	54.1 (80.7)	0.46	**0.013***
BASDAI 50 improvement, positive/total (%)	14/44 (32)	17/47 (36)	51/101 (50)	45/106 (42)	19/38 (50)	18/46 (39)	0.1	0.75
ASAS PR, positive/total (%)	8/52 (15)	8/59 (14)	36/119 (30)	35/125 (28)	21/67 (31)	23/90 (26)	0.09	0.09
ASAS 20 improvement, positive/total (%)	16/27 (59)	3/20 (15)	19/42 (45)	13/46 (28)	9/23 (39)	8/28 (29)	0.32	0.47

*$p<0.05$; $p3$: p-value for the comparison of first visits between the groups; $p4$: p-value for the comparison of last visits (follow-up period) between the groups For the follow-up period, $p=0.006$ between the ES and AS groups and $p=0.82$ between the ES and PS groups.
ES: enteropathic spondylitis; AS: ankylosing spondylitis; PS: psoriatic spondylitis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASAS: Assessment of SpondyloArthritis International Society; ASAS PR: Assessment of SpondyloArthritis International Society Partial Remission; IQR: interquartile range.

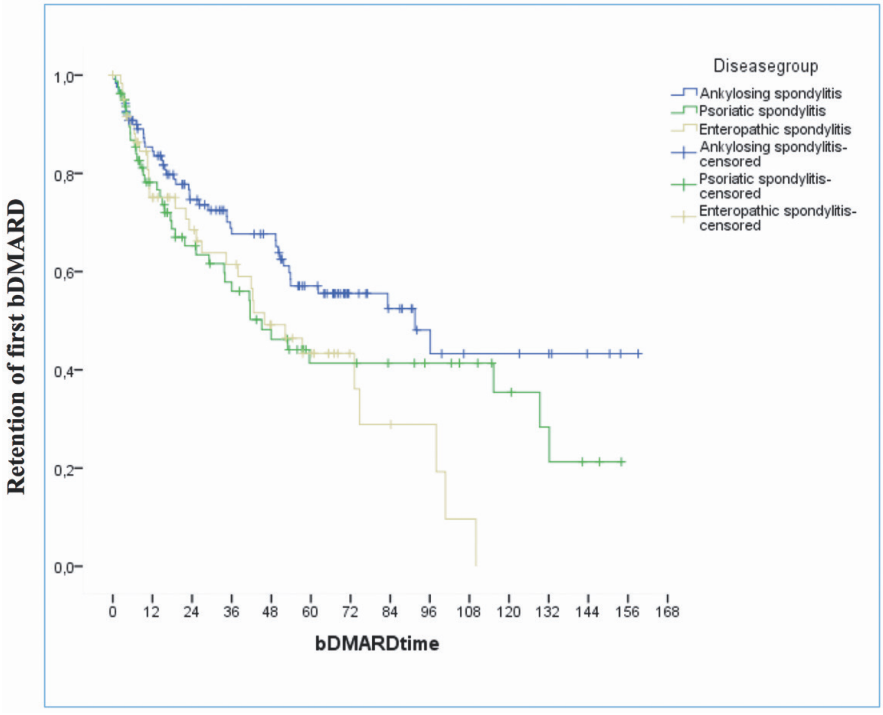

Fig. 2. Retention rate of the first bDMARD in all spondyloarthritis subgroups.
bDMARD: Biological disease-modifying anti-rheumatic drug. Log Rank $p=0.059$.

There was a marginal significant difference between the ES, AS and PS groups in terms of the retention rate of the first bDMARD (Log rank $p=0.059$) (Fig. 2). The median time to switching of the first bDMARD in the AS group was 91.5 months, while it was 45.1 months in the PS group and 45.9 months in the ES group. The cox regression analysis performed to identify the factors associated with the retention rate of first bDMARD in the ES patients revealed that the presence of UC was a significant predictor for drug switching (Hazard ratio [HR]: 7.0, 95% confidence interval [CI]: 1.15–42.3, $p=0.034$). Moreover, while the PGA-VAS score was found to be a significant predictive factor for bDMARD switching (HR: 1.05, 95% CI: 1.01–1.09, $p=0.015$), the disease duration was quite close to significance (HR: 0.8, 95% CI: 0.67–1.0, $p=0.057$).

Discussion

In the HUR-BIO registry, eSpA accounted for a small percentage (3.6%) of all SpA patients. A large majority of eSpA patients (71%) on bDMARD treatment had axial involvement with radiographic sacroiliitis. Resende *et al*. (11) described the Brazilian SpA cohort including 1,472 SpA patients and they reported that 3.2% of the patients were classified as eSpA and 60% of these eSpA patients had radiological sacroiliitis according to the mNY criteria. These rates were close to the rates of the present study; thus, both studies showed that eSpA patients were a small subgroup of all SpA patients and most of them had axial diseases. Although rates of peripheral and axial involvement in eSpA are different in the studies, peripheral involvement rate is higher than the rate of axial involvement. In the study by Chimenti *et al*. (12), 65% of eSpA patients had peripheral involvement, while 35% of the patients had axial involvement. In another study, the rate of only peripheral involvement was 53% in eSpA patients, while the rate of only axial involvement was 26% (13). A meta-analysis reported the rate of sacroiliitis as 10% and peripheral arthritis as 13% in IBD patients (14). In the present study, we evaluated the rate of sacroiliitis in the setting of patients using bDMARD. We should emphasise that eSpA patients with axial involvement require bDMARD treatment more than those having peripheral involvement. Similarly, Chimenti *et al*. (12) reported that eSpA patients with sacroiliitis were in need of bDMARD treatment more than the patients with peripheral arthritis.

Spondyloarthritis is a well-accepted concept which includes different subgroups such as AS, PS, and ES and these subgroups may have some similar clinical properties. In the present study, most of the clinical features, except for uveitis, were similar between the ES patients and the age- and disease duration-matched AS patients. IBD patients with peripheral involvement or espe-

cially with axial involvement develop uveitis (2, 13, 15). In a study, 70% of eSpA patients had axial involvement and the frequency of uveitis was 3.4%; however, the rate of uveitis was 23% in the AS patients (16). Indeed, the lower rate of uveitis in eSpA patients compared with AS patients is consistent with the literature.

High acute phase reactants are one of the markers that show disease activity in SpA patients (17, 18). However, an elevated ESR is present only in about 40–50% of patients with AS; thus, normal ESR levels do not comprehensively indicate active disease (19). In the present HUR-BIO cohort, all baseline disease activity and function scores were comparable in all SpA subgroups, except for acute phase reactants, particularly the ESR level. One of the reasons of high acute phase reactants in the ES patients might be related to bowel disease activity, rather than axial disease activity.

The rate of HLA-B27 positivity ranges from 36% to 80% in patients with IBD-associated SpA and seems to be a marker of progressive axial disease rather than the presence of sacroiliitis, in which HLA-B27-positivity is less likely (20, 21). In the present study, HLA-B27 positivity was found in 41% (11/27) of the patients with ES. Among these patients, HLA-B27 positivity was 54% in the CD patients and 29% in the UC patients. When considering the low frequency of HLA-B27 positivity in AS patients in Turkey (22), HLA-B27 positivity of 41% in the ES patients in our study may be due to different genetic and/or environmental factors in Turkey and it is an acceptable rate in ES patients in Turkey.

Regarding the IBD type, the number of UC and CD patients was similar (53% and 47%, respectively) in the present study. Actually, AS and sacroiliitis (symptomatic or not) are more commonly observed in patients with CD compared with those having UC in other studies. In our study, we found a slightly different rate in this subgroup from other studies (23-27). When we compared the demographic and clinical features of CD and UC patients, we found that family history of SpA was more common in the CD patients than in the UC patients (37% and 15% respectively, p=0.04). To the best of our knowledge, there is no study comparing CD and UC patients with sacroiliitis in the literature. However, there are two studies comparing CD and UC with respect to joint findings (13, 28). In these studies, family history of SpA was found to be 16% to 40% in CD patients and 9% to 39% in UC patients with joint findings. Considering that CD shows a more frequent familial pattern than UC (29), the rates we found are anticipated.

Management of patients with eSpA requires a treatment for both intestinal inflammation and musculoskeletal symptoms. For this purpose, corticosteroids, cDMARDs, and bDMARDs may be chosen to suppress inflammation in eSpA patients. In the present study, cDMARDs (more frequently sulphasalazine) were more preferred in the ES and PS patients compared with the AS patients. Besides suppressing joint symptoms, sulphasalazine may suppress bowel activity (30) in ES patients, while methotrexate is also preferred to suppress psoriasis exacerbation (31). In our study, 36% of the ES patients were using concomitant cDMARD, of whom 23% were using sulphasalazine and 11% were using methotrexate. In another study with similar results, 30% of the eSpA patients were treated with cDMARDs in combination with bDMARDs and sulphasalazine was the most frequently used cDMARD followed by methotrexate (32). These results are compatible with the literature.

Nowadays, TNF inhibitors (TNFi) are the gold-standard treatment for eSpA patients with IBD of whom symptoms are not suppressed with cDMARDs. Monoclonal TNFi, such as infliximab and adalimumab, are well studied and found to be effective in IBD patients and infliximab looks like the first-line treatment option for ES in the HUR-BIO registry. In the ES subgroup, although etanercept (TNF receptor antibody) was one of the treatment options as the first bDMARD (14%), the patients were switched from etanercept to monoclonal antibodies during the follow-up period and only 2% of the patients were using etanercept at the last outpatient visit. This is because etanercept is ineffective in CD (not studied in UC) and causes the development of IBD (33, 34).

While the treatment responses were similar in three SpA subgroups in the present study, the retention rate of the first bDMARD was marginally significantly different between these groups. Drug retention rate is an important outcome measure for treatment response and drug safety. Although there are studies on retention rates of bDMARDs in AS and PsA (35, 36), there is not enough data for eSpA. In studies, drug retention rates in axSpA patients starting their first TNFi treatments have ranged between 71–94% after 12 months (37, 38). This is in line with our findings for the ES, AS, and PS patients in whom the drug retention rates at 12-month follow-up were 75%, 84%, and 78%, respectively. The retention rates for the first TNFi were not different for SpA subtypes reported in the previous study of the HUR-BIO registry (39). In the present study, UC was 7 times more associated with the switching of the first bDMARD in comparison to CD. The retention rate of bDMARDs in eSpA has not been reported in the literature yet and further studies and controversies are needed on this subject.

In the present study, regarding the treatment responses evaluated by BASDAI 50 improvement, ASAS PR, and ASAS 20 improvement, there were no significant differences between the three SpA subgroups both at the first and last control visits. Although it seems difficult to identify the disease-specific factors among the axSpA groups in predicting the initial bDMARD treatment response, there were no significant differences between the groups in treatment responses. In the ES, AS, and PS groups, the rates of switching of the first bDMARDs were 50%, 36%, and 42%, respectively and ineffectiveness and side effects were the most common causes of switching. In the studies, switching rates of TNFi in SpA patients range between 22–44% and the most common causes have been reported as drug ineffectiveness and side effects (35, 40-43). While our rates of switch-

ing between bDMARDs in the AS and PS patients were compatible with the studies in the literature, although there is no data in the literature regarding ES, the switching rate was found higher in the ES group when evaluated as the SpA subgroup. Considering etanercept, which was the first initiated bDMARD in the ES group, the rate of ES patients using etanercept was 14%. The rate of switching from etanercept to another bDMARD might be expected to be a little higher in this group due to intestinal exacerbations rather than sacroiliitis.

There are some limitations in the present study. Firstly, there are missing data in several parameters due to retrospective nature of the study. Secondly, the sample size is small as it is a single-centre study. Thirdly, since the HUR-BIO registry database consists of patients using bDMARD, we could not evaluate patients who were not on bDMARD treatment. Fourthly, radiological assessment was evaluated by a single doctor (UK). Fifthly, escalation and loading doses for bDMARD were not known. Sixthly, we did not evaluate extraspinal involvement (such as dactylitis, enthesitis) that could have an effect on drug survival due to missing data. Lastly, level of IBD activity in the eSpA patients was unknown. On the other hand, an important strength of our study is that it presents data from the real-world clinical setting as our patients are routine clinic patients and this also increases the generalisability of our results.

In conclusion, a large majority of eSpA patients who were on bDMARD treatment had radiographic sacroiliitis, which we named as ES. ES patients had distinctive features that distinguish them from AS and PS patients. In the present study, the first bDMARD started in the ES group was mainly infliximab compared with the other groups. The retention rates for the first bDMARD between the three groups were marginally significant. The rate of switching between bDMARDs in the ES patients were slightly more than those in the AS and PS patients. The median time to switching of the first bDMARD in the AS patients was higher than those in the ES and PS patients. The treatment responses of the three groups were similar.

Key messages

- A large majority of enteropathic arthritis patients on bDMARD treatment had axial involvement.
- Enteropathic spondylitis patients had characteristic features that distinguish them from other SpA patients with spondylitis.
- Treatment responses and retention rates of bDMARDs were similar in all spondylitis subgroups.

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