RHEUMATOLOGY

Original article

Factors associated with remission at 5-year follow-up in recent-onset axial spondyloarthritis: results from the DESIR cohort

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Abstract

Objective. The factors contributing to long-term remission in axial SpA (axSpA) are unclear. We aimed to characterize individuals with axSpA at the 5-year follow-up to identify baseline factors associated with remission.

Methods. We included all patients from the DESIR cohort (with recent-onset axSpA) with an available Ankylosing Spondylitis Disease Activity Score–CRP (ASDAS-CRP) at 5-year follow-up. Patients in remission (ASDAS-CRP < 1.3) were compared with those with active disease by demographic, clinical, biological and imaging characteristics. A logistic model stratified on TNF inhibitor (TNFi) exposure was used.

Results. Overall, 111/449 patients (25%) were in remission after 5 years. Among those never exposed to TNFi, 31% (77/247) were in remission compared with 17% (34/202) of those exposed to TNFi. Patients in remission after 5 years were more likely to be male, HLA-B27+, have a lower BMI, and a higher education level. Baseline factors associated with 5-year remission in patients never exposed to TNFi included lower BASDAI [adjusted odds ratio (OR_a) 0.9, 95% CI: 0.8, 0.9) and history of peripheral arthritis (OR_a 2.1, 95% CI: 1.2, 5.3). In those exposed to TNFi, remission was associated with higher education level (OR_a 2.9, 95% CI: 1.6, 5.1), lower enthesitis index (OR_a 0.8, 95% CI: 0.7, 0.9), lower BASDAI (OR_a 0.9, 95% CI: 0.9, 0.9) and lower BMI (OR_a 0.8, 95% CI: 0.7, 0.9).

Conclusion. This study highlights the difficulty in achieving 5-year remission in those with recent-onset axSpA, especially for the more active cases, despite the use of TNFi. Socio-economic factors and BMI are implicated in the outcome at 5 years.

Key words: spondyloarthritis, remission, cohort, prognostic factor

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Rheumatology key messages

- This study revealed the difficulty in achieving 5-year remission in recent-onset axial spondyloarthritis (25% overall).
- Remission of disease activity in axial spondyloarthritis is more difficult to achieve in those with more active disease at baseline.
- Socio-economic factors, such as educational status and body mass index, are associated with long-term remission of disease.

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CLINICAL SCIENCE

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Introduction

SpA is a heterogeneous group of chronic inflammatory rheumatic diseases affecting mainly the spine but also presenting peripheral symptoms in the joints and entheses as well as extra-articular involvement [1] . The clinical course of axial SpA (axSpA) is highly variable [2] and can be characterized by ongoing axial inflammation and radiographic progression associated with restricted mobility of the spine, reduced function, and disability leading to impaired quality of life [3, 4]. Recommendations emerging from the Assessment of SpondyloArthritis international Society (ASAS)/EULAR group for managing axSpA have defined long-term health-related quality of life as the primary treatment goal [5], which emphasizes control of symptoms and inflammation.

In the past two decades, treat-to-target strategies have been included in clinical practice and are currently proposed in the field of axSpA [5, 6]. The aim is to reach and maintain a state of clinical remission or inactive disease [7]. Indeed, usually, remission refers to disease activity, and an inactive disease state can be considered a suitable proxy for remission. To assess disease activity, a reference tool is the Ankylosing Spondylitis Disease Activity Score–CRP (ASDAS-CRP), a composite index including clinical evaluation [back pain, patient global assessment of disease activity (PtGA)], rheumatologic data (duration of morning stiffness, peripheral joint pain/swelling) and a biologic marker of inflammation (CRP) [8]. This index allows for classifying patients as having inactive disease (score < 1.3) and low (score $\geq$1.3–<2.1), high (score $\geq$2.1–<3.5) or very high disease activity (score $\geq$3.5), with high discriminant capacity [9]. Although the definition of the target to be achieved in treat-to-target strategies is not agreed in axSpA, the ASDAS-CRP is often considered the most optimal tool [10], and a sustained score of <1.3 would be an appropriate target, because it would reduce the risk of subsequent structural damage progression [11].

Data on remission in axSpA are sparse [2], and identification of long-term remission factors (allowing for better understanding of the clinical course and adaptation of patient care) seems necessary but remains poorly studied [12–14]. The aims of this study were to assess the proportion of patients with recent-onset axSpA who were in remission according to ASDAS-CRP at 5-year follow-up, describe their characteristics in comparison with patients with active disease at that time, and especially to identify baseline factors associated with remission at 5-year follow-up.

Methods

Data source

For this analysis, 5-year follow-up data from the DESIR (*Devenir des Spondylarthropathies Indifférenciées Récentes*) cohort (NCT01648907) were used. The DESIR cohort has been previously described [15, 16]. Briefly, consecutive patients aged 18–50 years from 25 centres in France who had inflammatory back pain (evaluated by the Calin or Berlin criteria) [17, 18] that lasted $\geq$3 months but <3 years were included if the treating rheumatologist considered the symptoms suggestive of axSpA (score $\geq$5 on a scale of 0–10, with 0 = not suggestive and 10 = very suggestive). Visits were scheduled every 6 months during the first 2 years and annually thereafter.

The study was conducted according to good clinical practice guidelines and was approved by the appropriate local medical ethical committees (*Comité de Protection des Personnes Ile de France III*). All patients gave their written informed consent at their inclusion in the cohort. A detailed description of the study protocol is available at the DESIR website (http://www.lacohorte desir.fr/desir-in-english/). The research proposal for this particular analysis was approved by the scientific committee of the DESIR cohort.

Study population and disease activity assessment

We included all patients from the DESIR cohort for whom data on ASDAS-CRP at 5 years [i.e. Month 60 (M60)] and exposure to TNF inhibitors (TNFis) during the study period were available. The primary outcome was remission at M60, defined by ASDAS-CRP < 1.3.

Data collection

Relevant demographic, socio-economic, clinical and environmental information was obtained at baseline (M0) and 5-year follow-up (M60), as indicated in Table 1. No patient had TNFi exposure at inclusion, but this exposure was recorded over the course of the study. Exposure to other classes of biologics, in particular IL 17 inhibitors (IL17is), was not studied because the marketing authorization for SpA in France was obtained after the study period. 'History' variables are cumulative variables and correspond to a history of dactylitis, arthritis, psoriasis, IBD or uveitis since disease onset (i.e. inflammatory back pain onset). ASAS20 and ASAS40 response criteria were calculated between M60 and M0.

Statistical analyses

Categorical data are reported as number (percentage). Quantitative data are reported as median with 25–75% interquartile range or mean (S.D.). Patients considered in remission were compared with those not in remission at M60 according to their main characteristics (demographic, clinical, biological and imaging characteristics).

Relevant characteristics of included and non-included patients (due to missing data on ASDAS-CRP score and TNFi exposure) were compared at M0. The association between baseline factors and remission at 5-year follow-up was estimated by univariate and multivariate analyses. Variables associated with the outcome at $P \leq 0.10$ on univariate analysis were included in a multivariate model. Variables highly correlated with one

TABLE 1 Features of study population at 5-year follow-up according to remission or not status, with stratification on TNF inhibitor exposure

M60 factors	M60 remission (n = 111)		M60 active disease (n = 338)	
	Never exposed to TNFi n = 77 (69.4%)	Exposed to TNFi during follow-up n = 34 (30.6%)	Never exposed to TNFi n = 170 (50.3%)	Exposed to TNFi during follow-up n = 168 (49.7%)
Demographic characteristics at M60				
Age [mean (s.d.)]	37.8 (8.3)	36.1 (8.2)	39.8 (8.6)	39.5 (9.0)
Males	42 (54.6)	24 (70.6)	71 (41.8)	69 (41.1)
Ethnicity				
Caucasian	74 (96.1)	31 (91.2)	159 (93.5)	146 (86.9)
Black Africa	1 (1.3)	2 (5.9)	2 (1.2)	3 (1.8)
Asia	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)
Maghreb	1 (1.3)	0 (0.0)	5 (2.9)	13 (7.7)
Other	1 (1.3)	1 (2.9)	2 (1.2)	5 (3.0)
Education level			(/169)	
Primary school	0 (0.0)	1 (2.9)	2 (1.2)	0 (0.0)
Secondary school	16 (20.8)	8 (23.5)	58 (34.3)	84 (50.0)
University for ≤3 years	27 (35.1)	8 (23.5)	56 (33.1)	53 (31.5)
University for >3 years	34 (44.2)	17 (50.0)	53 (31.4)	31 (18.5)
BMI [mean (s.d.)]	23.5 (3.6) (/76)	23.8 (3.2)	24.4 (3.9) (/166)	25.9 (4.52) (/165)
Active smoking	20 (26.0)	11 (32.4)	51 (/169) (30.0)	62 (36.9)
Clinical and biological characteristics at M60				
ASAS criteria	60 (77.9)	28 (82.3)	115 (67.7)	114 (67.9)
HLA-B27+	58 (75.3)	26 (76.5)	108 (63.5)	92 (54.8)
History of dactylitis[a]	17 (22.1)	7 (20.6)	34 (20.0)	41 (24.4)
History of peripheral arthritis[a]	1 (/76) (1.3)	0 (0.0)	7 (/167) (4.2)	8 (/166) (4.8)
Tender joints [mean (s.d.)]	0.2 (0.7) (/76)	0.4 (1.0)	2.3 (4.4) (/165)	4.4 (8.4) (/166)
Swollen joints [mean (s.d.)]	0.0 (1.1) (/76)	0.0 (0.0)	0.1 (0.4) (/167)	0.1 (0.6) (/166)
Enthesitis index [mean (s.d.)]	0.6 (1.1) (/76)	0.1 (0.5)	2.7 (4.4) (/165)	4.5 (5.7) (/163)
History of psoriasis[a]	0 (0.0)	2 (5.9)	2 (1.2)	2 (1.2)
History of IBD[a]	0 (0.0)	0 (0.0)	2 (1.2)	4 (2.4)
History of uveitis[a]	2 (2.6)	1 (2.9)	9 (5.3)	5 (/166) (3.0)
PtGA (mean (s.d.))	0.7 (0.9)	1.0 (1.1)	4.1 (2.3)	3.3 (2.2) (/166)
PhGA [mean (s.d.)]	0.9 (1.1) (/76)	0.8 (0.9) (/33)	2.9 (2.0) (/167)	5.4 (2.0)
CRP	2.2 (1.4)	1.9 (1.0) (/33)	7.4 (15.7)	5.1 (6.1)
ASDAS-CRP [mean (s.d.)]	1.0 (0.2)	0.9 (0.2)	2.4 (0.7)	2.4 (0.7)
BASDAI [mean (s.d.)]	11.4 (7.6)	9.2 (6.2)	37.6 (17.8)	41.9 (19.0)
BASFI [mean (s.d.)]	5.0 (5.6)	6.2 (9.1)	23.8 (20.8) (/167)	37.8 (20.9)
ASAS20 response criteria	49 (63.6)	30 (88.2)	48 (28.9) (/166)	75 (44.9) (/167)
ASAS40 response criteria	43 (55.8)	29 (85.3)	29 (17.3) (/168)	43 (25.7) (/167)
Imaging criteria at M60				
X-ray sacroiliitis	18 (/75) (24.0)	11 (/30) (36.7)	37 (/132) (24.3)	41 (/151) (27.2)
MRI active sacroiliitis	11 (/30) (36.7)	9 (/22) (40.9)	14 (/47) (29.8)	14 (/65) (21.5)
Treatment exposure at M60				
NSAIDs	42 (54.5)	10 (29.4)	137 (80.6)	106 (63.1)
CSs	4 (5.2)	0 (0.0)	5 (2.9)	19 (11.3)
csDMARDs	0 (/76) (0.0)	0 (0.0)	0 (/167) (0.0)	0 (0.0)

Data are n (%) unless indicated. Italics indicate the number of patients with available data. TNFi: TNF inhibitor; M60: month 60; ASAS: Assessment of SpondyloArthritis international Society; tender joint count/53; swollen joint count/28; Enthesitis index/39 (concise Mander Enthesitis score with gradation); PtGA: patient's global assessment of disease activity/ 10; PhGA: physician's global assessment of disease activity/10; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index (/100); BASFI: Bath Ankylosing Spondylitis Functional Index (/100); csDMARD: conventional synthetic DMARD. [a]History since inflammatory back pain onset (before inclusion or during the study).

another were excluded from the multivariate analyses to ensure independence of identified factors. Multivariate analysis involved using logistic regression stratified on TNFi exposure, estimating adjusted odds ratios (ORₐs) and 95% CIs. Patients were considered exposed during follow-up if they had received a TNFi for >3 months at any time during the study period. Other patients were considered never exposed.

To assess the sensitivity of the estimated OR$_a$s, we performed the following additional analyses: (1) a logistic multivariate analysis stratified on TNFi exposure among patients with an axSpA diagnosis confirmed by a rheumatologist at M60 (the diagnosis of SpA was retained at M60 if the rheumatologist had confidence in the diagnosis of ≥8/10); (2) a logistic multivariate analysis stratified on TNFi exposure among those meeting the ASAS criteria at M60; (3) a post-hoc logistic multivariate analysis stratified on TNFi exposure among those meeting the ASAS criteria on MRI (X-ray + or X-ray −) at M0; and (4) a multivariate case–control analysis with matching TNFi exposure. In this analysis, we previously calculated the number of participants needed and then matched 1 case (patient in remission) with 2 controls (patient not in remission).

$P < 0.05$ was considered statistically significant. No corrections for multiple comparisons were performed. All analyses were performed with SAS Enterprise Guide v7.1 (SAS Institute Inc., Cary, NC, USA).

Results

Description of all included patients and patients in remission

A total of 614 patients were followed in the DESIR cohort at M60. After excluding those with missing data on ASDAS-CRP ($n = 163$) and TNFi exposure ($n = 2$), we retained 449 (73%) patients for analysis, including 247 (55%) never exposed to TNFi [mean age 39.2 (8.6) years; 46% men] and 202 (45%) exposed to TNFi for at least 3 months at any time during follow-up [mean age 38.9 (8.9) years; 46% men] (Fig. 1). In the latter group, 180 (89%) patients remained on TNFi at M60. Included and non-included patients had similar baseline characteristics (Supplementary Table S1, available at *Rheumatology* online).

Overall, 111 (25%) patients were in remission at M60: 77 (69%) never exposed and 34 (31%) exposed to TNFi during the study period. Specifically, among the 247 patients never exposed to TNFi, 77 (31%) were in remission, whereas among the 202 patients exposed to TNFi during the study period, 34 (17%) were in remission (33 of the 34 remained on TNFi at M60). The mean duration of exposure to TNFi was 2.9 (1.9) years [median: 3.7 (interquartile range 0.7–4.7)] and 3.4 (1.6) years [median: 4.2 (2.2–4.7)] in the remission and non-remission group at M60. A total of 32 patients [mean age 32.3 (8.2) years, 62% males, 69% HLA B27+] were in drug-free remission [never exposed to a TNFi, no NSAIDs nor conventional synthetic DMARDs (csDMARDs) at M60]. Table 1 presents characteristics of the included patients according to their remission/non-remission status. Patients in remission *vs* non-remission at 5-year follow-up were

FIG. 1 Flow-chart for analytical approach
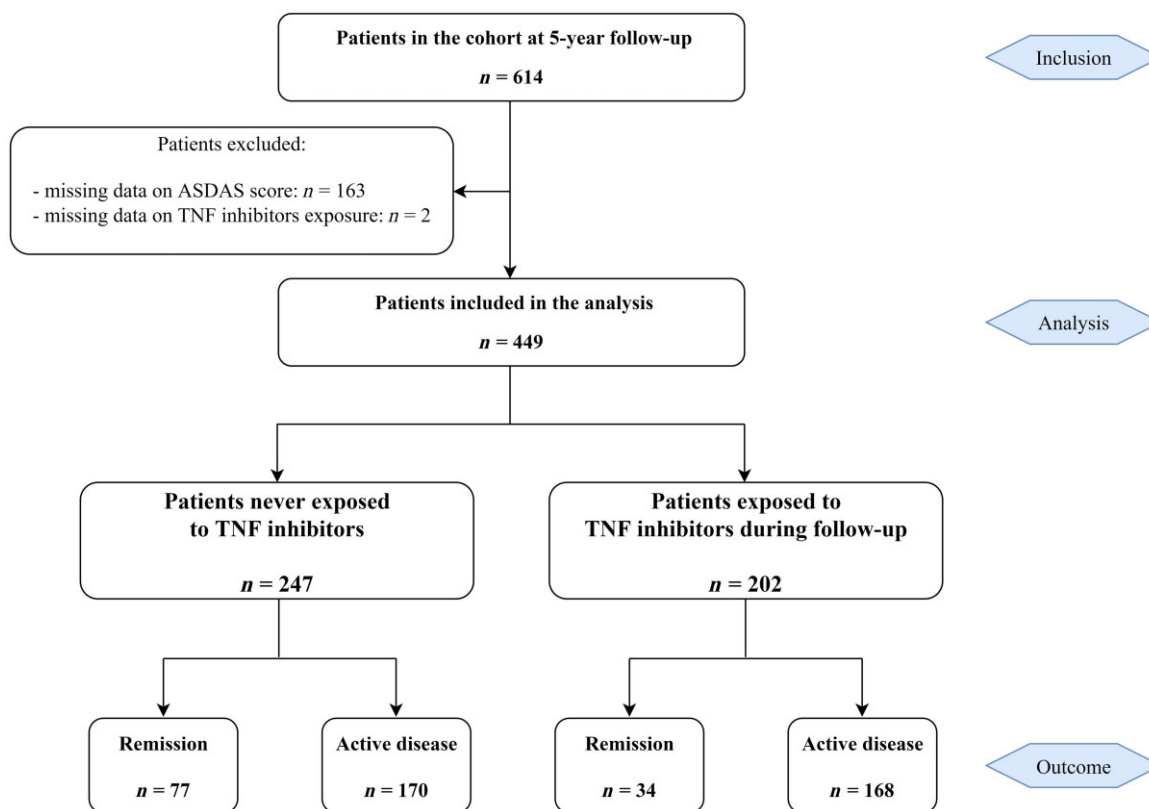
ASDAS: Ankylosing Spondylitis Disease Activity Score; TNF: tumor necrosis factors.

more frequently men; had a higher education level, lower BMI, and higher incidence of HLA-B27; and more frequently met the ASAS criteria. As expected, they had lower CRP, enthesitis index, number of tender and swollen joints and total BASDAI but also lower NSAID and TNFi use. ASAS20 and ASAS40 response criteria were achieved in 39.9% ($n = 97$) and 29.4% ($n = 72$) of patients, respectively, among those never exposed to TNFi. They were achieved in 52.2% ($n = 105$) and 35.8% ($n = 72$) of patients, respectively, among those exposed to TNFi during follow-up.

Baseline factors associated with remission at 5-year follow-up

On univariate analyses, among patients never exposed to TNFi, patients with remission *vs* non-remission more frequently had higher education level ($P < 10^{-4}$); a history of peripheral arthritis ($P = 0.03$); lower enthesitis index ($P = 0.03$), PtGA ($P < 10^{-3}$) and physician's global assessment of disease activity (PhGA) ($P < 10^{-3}$); and lower ASDAS-CRP ($P < 10^{-3}$), BASDAI ($P < 10^{-3}$) and BASFI ($P < 10^{-3}$) at baseline (Table 2). Among patients exposed to TNFi during follow-up, patients with remission *vs* non-remission more frequently were men ($P < 10^{-3}$) and had higher education level ($P < 10^{-4}$), HLA-27 positivity ($P = 0.02$) and active sacroiliitis on MRI ($P = 0.03$) as well as lower baseline BMI ($P = 0.02$), enthesitis index ($P < 10^{-3}$), PtGA ($P < 10^{-3}$), BASDAI ($P < 10^{-3}$) and BASFI ($P < 10^{-3}$) (Table 2).

On multivariate analysis, among patients never exposed to TNFi, baseline factors associated with 5-year remission were a history of peripheral joint arthritis (OR$_a$ 2.1, 95% CI: 1.2, 5.3) and reduced BASDAI score (OR$_a$ 0.9, 95% CI: 0.8, 0.9) (Table 3). Among patients exposed to TNFi, baseline factors associated with 5-year remission were higher educational attainment (OR$_a$ 2.9, 95% CI: 1.6, 5.1) and reduced enthesitis index (OR$_a$ 0.8, 95% CI: 0.7, 0.9), BASDAI (OR$_a$ 0.9, 95% CI: 0.9, 0.9) and BMI (OR$_a$ 0.8, 95% CI: 0.7, 0.9).

Sensitivity analyses

The results of the multivariate analysis among patients with an axSpA diagnosis confirmed by a rheumatologist at M60 ($n = 374$) and those meeting the ASAS criteria at M60 ($n = 317$) were globally consistent with those of the main analysis; only increased BMI was no longer significant ($P = 0.06$) in patients exposed to TNFi, although OR$_a$s were unchanged (Supplementary Table S2, available at *Rheumatology* online). In the same way, the results of the multivariate analysis among those who met the ASAS criteria on MRI at M0 ($n = 198$) remained globally consistent. In the subgroup of patients exposed to TNFi, HLA-B27+ was also significantly associated with remission at 5-years (Supplementary Table S2, available at *Rheumatology* online).

The results of the multivariate matched case–control analysis ($n = 333$) were consistent with those of the main

analysis (Supplementary Table S3, available at *Rheumatology* online).

Discussion

Using real-life data from the DESIR cohort with recent-onset axSpA, we estimated that 25% of cases overall were in remission at 5 years: 31% of those never exposed to TNFi and 17% of those exposed to TNFi, respectively. Long-term remission was more difficult to achieve in those with more active disease at baseline (high BASDAI and enthesitis index). Socio-economic factors (including educational status) and BMI were also implicated in the outcome at 5 years.

Our study highlights the difficulty in achieving 5-year remission in recent-onset axSpA. We observed an overall remission rate similar to that previously described in the DESIR cohort at the 2-year follow-up (24%) [14], but also in other observational studies of SpA patients (21% to 22.5%) [19, 20]. In randomized controlled trials, remission rates were higher [21]: among unexposed patients, when disease was treated with NSAIDs, remission rates ranged from 9.1% to 17.6% at 6 weeks and 19.6% to 35.3% at 28 weeks [22, 23]; among exposed patients, remission rates ranged from 16% to 61.9% [23, 24]. However, unlike in our study, these populations were strictly selected and had a limited follow-up. In our real-world data, few patients in the TNFi group were in remission, while most were still exposed at M60, perhaps reflecting limits in terms of response to TNFi, with patients who responded but not according to the stringent definition of ASAS remission. Nevertheless, we note that the proportions of patients meeting the ASAS20 and ASAS40 improvement criteria, which are considerably less stringent, also remained low in our study. Of note, 170 patients were not in remission at M60 but had never been exposed to TNFi, raising the question of whether some patients were under-treated at that time in France, especially those with non-radiographic forms, not covered by marketing authorization. We may also question our definition of remission in real life: some patients (and their treating physicians) might be satisfied without achieving an ASDAS-CRP < 1.3; others might have treatment objectives based on other factors (especially other patient-reported outcomes) [25–27]. Finally, a substantial proportion of patients (7%) did not require NSAIDs, csDMARDs or TNFi to be in remission. The concept of drug-free remission is a well-documented occurrence in rheumatoid arthritis (RA) (10–15% of patients) [28–30], but has been poorly investigated in axSpA. Our study suggests that some patients with a particular profile (notably young men with HLAB27+) may spontaneously achieve remission.

Patients in remission after 5 years were more likely to be male, HLA-B27+, have a lower BMI and a higher education level. These results are consistent with those reported earlier in RA [31, 32], but also SpA [14, 33]. Our findings are clinically meaningful because they

TABLE 2 Comparison of baseline characteristics according to remission or not status at 5-year follow-up after stratifying on TNF inhibitor exposure

Baseline factors	Never exposed to TNFi ($n = 247$)			Exposed to TNFi during follow-up ($n = 202$)		
	M60 remission $n = 77$ (31.2%)	M60 active disease $n = 170$ (68.8%)	*P*-value	M60 remission $n = 34$ (16.8%)	M60 active disease $n = 168$ (83.2%)	*P*-value
Baseline demographic characteristics						
Age [mean (s.d.)]	32.7 (8.3)	34.7 (8.6)	0.08	31.0 (8.2)	34.4 (9.0)	0.05
Males	42 (54.5)	71 (41.8)	0.06	24 (70.6)	69 (41.1)	**<10⁻³**
Ethnicity			0.46			0.28
Caucasian	74 (96.1)	159 (93.5)		31 (91.2)	146 (86.9)	
Black Africa	1 (1.3)	2 (1.2)		2 (5.9)	3 (1.8)	
Asia	0 (0.0)	2 (1.2)		0 (0.0)	1 (0.6)	
Maghreb	1 (1.3)	5 (2.9)		0 (0.0)	13 (7.7)	
Other	1 (1.3)	2 (1.2)		1 (2.9)	5 (3.0)	
Education level		(*/169*)	**<10⁻⁴**			**<10⁻⁴**
Primary school	0 (0.0)	2 (1.2)		1 (2.9)	0 (0.0)	
Secondary school	16 (20.8)	58 (34.3)		8 (23.5)	84 (50.0)	
University for ≤3 years	27 (35.1)	56 (33.1)		8 (23.5)	53 (31.6)	
University for >3 years	34 (44.2)	53 (31.4)		17 (50.0)	31 (18.4)	
BMI [mean (s.d.)]	23.0 (3.6) (*/76*)	23.9 (4.0) (*/169*)	0.10	22.8 (3.2)	24.6 (4.4) (*/167*)	**0.02**
Active smoking	23(*/76*) (30.3)	56 (*/169*) (33.1)	0.65	13 (38.2)	67 (*/167*) (40.1)	0.83
Baseline clinical and biological characteristics						
ASAS criteria	58 (75.3)	109 (64.1)	0.08	26 (76.5)	104 (61.9)	0.11
HLA-B27+	58 (75.3)	108 (63.5)	0.06	26 (76.5)	92 (54.8)	**0.02**
History of dactylitis[a]	12 (15.6)	17 (10.0)	0.21	5 (14.7)	25 (14.88)	0.97
History of peripheral arthritis[a]	19 (24.7)	23 (*/169*) (13.6)	**0.03**	12 (35.3)	43 (*/167*) (25.8)	0.26
Tender joints [mean (s.d.)]	1.6 (1.9) (*/76*)	5.1 (5.0)	0.44	2.7 (5.2)	5.9 (8.7)	**0.04**
Swollen joints [mean (s.d.)]	0.2 (1.4) (*/76*)	0.0 (0.2)	0.34	0.3 (0.6)	0.2 (1.1)	0.74
Enthesitis index (mean (s.d.))	2.1 (4.6)	3.5 (5.1)	**0.03**	1.6 (2.9)	6.0 (5.9) (*/166*)	**<10⁻³**
History of psoriasis[a]	14 (18.2)	24 (14.1)	0.41	7 (20.6)	31 (18.4)	0.77
History of IBD[a]	3 (3.9)	9 (5.3)	0.63	2 (5.9)	13 (7.7)	0.71
History of uveitis[a]	5 (6.5)	21 (12.3)	0.17	4 (11.8)	10 (5.9)	0.23
PtGA [mean (s.d.)]	3.4 (2.6)	4.5 (2.5) (*/168*)	**<10⁻³**	5.0 (2.2)	6.1 (2.3) (*/166*)	**<10⁻³**
PhGA [mean (s.d.)]	3.0 (2.0)	3.7 (1.9)	**<10⁻³**	4.8 (2.2)	5.4 (2.0)	0.10
High CRP	14 (*/72*) (19.4)	33 (*/164*) (20.1)	0.90	18 (*/33*) (54.5)	62 (*/165*) (38.0)	0.08
ASDAS-CRP [mean (s.d.)]	2.0 (0.9) (*/72*)	2.3 (0.8) (*/161*)	**<10⁻³**	2.8 (0.9) (*/33*)	3.1 (0.9) (*/161*)	0.13
Remission (ASDAS-CRP <1.3)	18 (*/72*) (25.0)	12 (*/161*) (7.4)	0.24	1 (*/33*) (3.0)	1 (*/161*) (0.6)	0.22
BASDAI [mean (s.d.)]	29.7 (19.8)	38.3 (18.2) (*/169*)	**<10⁻³**	43.0 (17.5)	53.8 (17.2) (*/167*)	**<10⁻³**
BASFI [mean (s.d.)]	15.8 (18.4)	23.7 (20.1) (*/166*)	**<10⁻³**	27.5 (19.1)	41.1 (22.1)	**<10⁻³**
Baseline imaging criteria						
X-ray sacroiliitis	11 (14.3)	28 (*/167*) (24.3)	0.62	11 (32.3)	36 (*/164*) (21.9)	0.20
MRI active sacroiliitis	27 (*/76*) (35.5)	60 (*/169*) (35.5)	0.99	20 (58.8)	62 (*/163*) (38.1)	**0.03**
Baseline treatment exposure						
NSAID exposure	70 (*/75*) (93.3)	154 (*/168*) (91.1)	0.56	32 (94.1)	145 (86.3)	0.22
CS exposure	6 (7.8)	11 (6.5)	0.70	5 (14.7)	34 (*/167*) (20.4)	0.41
csDMARD exposure	9 (11.7)	12 (7.1)	0.23	5 (14.7)	34 (20.4)	0.45

Data are *n* (%) unless indicated. Italics indicate the number of patients with available data. Bold text indicates statistically significant results. TNFi: TNF inhibitor; M60: month 60; ASAS: Assessment of SpondyloArthritis international Society; csDMARD: conventional synthetic DMARD. [a]Since inflammatory back pain onset (before inclusion).

TABLE 3 Baseline factors associated with remission at 5-year follow-up (multivariate analysis) after stratifying on TNF inhibitor exposure

Baseline factors	Never exposed to TNFi (n = 247)		Exposed to TNFi during follow-up (n = 202)	
	OR$_a$ (95% CI)	P-value	OR$_a$ (95% CI)	P-value
Age	0.9 (0.9, 1.0)	0.34	0.9 (0.9, 1.0)	0.77
Sex (ref: male)	0.9 (0.6, 2.2)	0.61	2.0 (0.7, 5.6)	0.16
Education level	1.3 (0.9, 1.9)	0.14	**2.9 (1.6, 5.1)**	**<10^{-4}**
BMI	1.4 (0.9, 1.1)	0.32	**0.8 (0.7, 0.9)**	**0.05**
Active smoking	2.8 (0.4, 1.6)	0.57	1.2 (0.5, 3.0)	0.71
HLA-B27+	1.3 (0.7, 2.6)	0.43	2.7 (0.9, 7.6)	0.06
History of peripheral arthritis[a]	**2.1 (1.2, 5.3)**	**0.01**	2.3 (0.8, 6.5)	0.12
Enthesitis index	0.9 (0.8, 1.1)	0.45	**0.8 (0.7, 0.9)**	**0.01**
BASDAI	**0.9 (0.9, 0.9)**	**0.01**	**0.9 (0.9, 0.9)**	**0.02**

Bold text indicates statistically significant results. TNFi: TNF inhibitor; OR$_a$: adjusted odds ratio; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index (/100). [a]Past history since inflammatory back pain onset (before inclusion).

highlight low baseline disease activity associated with long-term remission.

In our study, less-educated patients were not only less frequently prescribed a biologic but also had greater disease activity with TNFi at 5 years than more-educated patients. Although the causality of this association is difficult to determine, several factors may be involved, such as access to rheumatologists, health literacy, adherence to treatment, or severity of the disease [33]. Moreover, among patients exposed to TNFi, the factors associated with long-term remission we identified, such as lower BMI, were well-known predictors of good response to TNFi [34–37]. However, male sex and no smoking were not significantly associated with remission in our multivariate analysis [38, 39]. In previous studies, when measured with the ASDAS-CRP, disease activity did not differ between men and women [40, 41]. Furthermore, although a link between smoking, inflammation and structural damage in early stages of axSpA has been suggested [21, 42], the effect of smoking on long-term remission is not clear, and several studies have failed to find this association for all patients (association only in men and blue-collar patients) [43, 44].

The limitations of this study include the cross-sectional nature of the outcome measure: ASDAS-CRP was assessed at a single time point. However, although axSpA may have flares and remission, a study using data from the DESIR cohort has shown that in >90% of cases, disease activity trajectories are stable over the follow-up [2]. We could not account for exposure to other classes of biologics, in particular IL17i, which received marketing authorization for SpA after the study period. Thus, the real-world remission rate in axSpA may be greater than the 25% we found. In addition, patients with TNFi exposure could have received the drug at any time during the 5 years and not necessarily just at 5 years; however, 89% of that group was still exposed to the TNFi at M60.

This study has several strengths. To our knowledge, this is the first real-world study dedicated to analyzing initial factors in recent onset axSpA associated with long-term remission. Our study involved a large patient sample and offered the opportunity to test many and robust factors at this crucial stage of the disease evolution. To better account for the interaction between the different remission-associated factors and the use of biologics, we stratified our analyses on TNFi exposure. Finally, several sensitivity analyses were performed and supported the integrity of our results.

Conclusion

This study reveals the difficulty in achieving 5-year remission in recent-onset axSpA, especially in those with more active disease at baseline. Socio-economic factors and BMI are associated with long-term remission of disease. In the era of personalized medicine, our results can guide clinicians in providing more targeted care to patients with axSpA by identifying early those at increased risk for long-term activity. Whether the remission rate could be changed with the introduction of therapeutic classes other than TNFi, already available and available in the near future, remains unknown.

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Data availability statement

All relevant data are reported in the article. Additional details can be provided by the corresponding author upon reasonable request.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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