The adherence to ASAS classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents in axial spondyloarthritis

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Abstract

Objective

To determine the adherence of practicing rheumatologists, before and after an educational project, to Assessment of SpondyloArthritis international Society (ASAS) classification criteria and to ASAS recommendations for the use of anti-tumor necrosis factor (TNF)-alpha agents in patients with axial spondyloarthritis (SpA).

Methods

The project involved 53 rheumatologists attending 2 educational meetings on an update of SpA. Each meeting included interactive sessions on 1) clinical cases, 2) clinimetric evaluation, including ASAS core set for daily practice and 3) imaging. Diagnostic and therapeutic approach of each participant was tested using short clinical cases, obtained from real-life rheumatology settings, at the beginning and at the end of this educational project. Each case for diagnostic (n=10) or therapeutic purpose (n=10) had 10 possible choices. Each participant gave a score from 0 (total disagreement) to 10 (total agreement) for each choice.

Results

At baseline, the rheumatologists had an excellent agreement with ASAS classification criteria for axial SpA and anti-TNF-alpha treatment according to ASAS recommendations with a further significant improvement after the educational programme. In axial SpA cases with acute anterior uveitis (AU) or Crohn's disease, anti-TNF-alpha treatment was indicated mainly as monoclonal anti-TNF antibody. In presence of elevated levels of CRP, anti-TNF option has been considered useful.

Conclusion

Practicing rheumatologists had a satisfying adherence to ASAS classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents for patients with axial SpA. Extra-articular manifestations and other variables might play a role in the decision-process of the management of axial SpA.

Key words

axial spondyloarthritis, ankylosing spondylitis, anti-TNF-alpha agents

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Significance and innovation of this study

- The present study deals with the adherence to Assessment of SpondyloArthritis international Society (ASAS) classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents in patients with axial spondyloarthritis (SpA) in the rheumatological clinical practice.
- Practicing rheumatologists have a satisfying adherence to ASAS classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents for patients with axial SpA.
- Educational projects further improve this adherence.
- Extra-articular manifestations and other variables might play a role in the decision-process of the management of axial SpA.

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Introduction

The diagnosis of ankylosing spondylitis (AS), a chronic, progressive, disabling disease with an important economic impact, is often missed and markedly delayed (1, 2).

The Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial spondyloarthritis (SpA) (3) encompass both patients with AS according to New York (NY) modified criteria (4) and patients without definite radiographic sacroiliitis, also referred to as non-radiographic axial SpA (5).

Although the prevalence of axial SpA in real life rheumatology setting could affect the post-test probability of the disease, these classification criteria should also perform quite well as diagnostic criteria if applied by rheumatologists (1). Moreover these criteria served as a basis for an extension of the use of tumor necrosis factor (TNF)-alpha blockers, effective in the management of AS (6), to the non-radiographic stage of axial SpA. In fact ASAS has developed recommendations for the use of anti-TNF-alpha agents taking into account the new axial SpA criteria (7). In this context, ASAS and the European League against Rheumatism (EULAR) developed recommendations for the management of AS, but the project group unanimously agreed that these recommendations can equally be applied to patients with non-radiographic axial SpA (8). Most national recommendations follow the international ASAS recommendations, contributing to comparable access to anti-TNF-alpha treatment across countries (9). Rheumatologists considered both disease activity and severity to be determinants of starting TNF blockers, but their decision could be in disagreement with ASAS recommendations (9, 10, 11), confirming the need for continued exchange among the medical community to increase awareness of the ASAS recommendations.

The aim of the present study was to determine the adherence of practicing rheumatologists, before and after an educational project, to ASAS classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents in patients with axial SpA.

Patients and methods

The project involved 53 Italian rheumatologists attending 2 educational meeting on an update of SpA according to the Italian regulation on Continuous Medical Education. All rheumatologists were invited to join this educational meeting on the basis of their experience with axial SpA, including non-radiographic SpA, and their availability to use anti-TNF-alpha drugs. These educational meetings were held in 2012 (30th-31st March and 28th-29th September). Each meeting included interactive sessions on 1) clinical cases (discussed in small groups focused on different skills in diagnostic and therapeutic field), 2) clinimetric evaluation including ASAS core set for daily practice (*i.e.* ASAS response criteria, AS Disease Activity Score, Bath AS Metrology Index, Bath AS Disease Activity Index, Bath AS Functional Index) (5) and 3) imaging (x-ray, MRI, ultrasound). In the interval between the 1st and the 2nd meeting, the participants could download the scientific contents of the project and were invited to submitted clinical cases about axial SpA to be discussed during the second meeting.

Diagnostic and therapeutic approach of each participant was tested using short clinical cases, obtained from real-life rheumatology settings, at the beginning (March) and at the end (September) of this educational project in a plenary session. Each case for diagnostic (n=10) or therapeutic purpose (n=10) had 10 possible choices. Votes for agreement or disagreement were performed anonymously by each participant, using an *iPad* Operating System, giving a score from 0 (total disagreement) to 10 (total agreement) for each choice. Case for diagnostic purpose included the following choices: 1) axial SpA fulfilling ASAS criteria (3); 2) axial SpA fulfilling NY criteria (4); 3) psoriatic arthritis fulfilling the ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria (13); 4) hip osteoarthritis; 5) spine osteoarthritis; 6) fibromyalgia; 7) lumbar disc herniation; 8) infective disciitis; 9) Diffuse Idiopathic Skeletal Hyperostosis (DISH); 10) facet joints arthrosis.

Cases for therapeutic purpose included the following choices: 1) at least

two NSAIDs for at least 3 months at maximum recommended dose unless contraindicated; 2) at least two NSAIDs over a 4-week period in total at maximum recommended dose unless contraindicated; 3) systemic glucocorticoids (prednisone <10 mg/daily); 4) corticosteroid injections of sacroiliac joints; 5) short (2–3 weeks) treatment with systemic glucocorticoids (prednisone ≥10 to 25 mg/daily); 6) physical therapy with supervised exercises, land or water based, individually or in a group; 7) sulfasalazine (2–3 gr/daily); 8) methotrexate (up to 15–20 mg/weekly); 9) recombinant fusion protein of human soluble TNF-alpha receptor; 10) monoclonal anti-TNF-alpha antibody.

Statistical analysis

Continuous variables were analysed by Mann-Whitney U-test for unpaired data or Wilcoxon *signed-rank* test for paired data. The results were presented as median (25^{th}–75^{th} percentile). We interpreted the agreement in the following way: values in the interval 9–10 represented excellent agreement, in 7–8 represented substantial agreement, in 5–6 represented moderate agreement, in 3–4 represented fair agreement, and in 0–2 represented poor agreement. *p*-values less than 0.05 were considered significant. All statistical analyses were performed using statistical software Prism 5 for Windows.

Results

The characteristics of the 53 rheumatologists who participated in the study were: M/F = 33/20; age (median/range) = 43/30–62 years; rheumatology professional activity duration (median/range) = 13/1–31 years.

In the 10 real-life cases examined for diagnostic purpose, the adherence of rheumatologists to ASAS classification criteria for axial SpA, before and after the educational project, is shown in Table I. The axial-SpA cases 1, 2, 3 and 5 fulfilled ASAS criteria, while only case 4 fulfilled both ASAS and modified NY criteria. At baseline, the rheumatologists had an excellent agreement with ASAS classification criteria for axial SpA with a further significant improvement after the educational program in cases 1, 2, 3. In cases 1, 2, 3 and 5 the initial level of agreement with modified NY criteria was fair/poor and it was further reduced after the educational program. In the remaining non-axial SpA cases, the rheumatologists correctly had a poor agreement with ASAS or NY criteria.

In the 10 real-life cases examined for therapeutic purpose, the treatment options in non-radiographic, radiographic and undifferentiated axial SpA, before and after the educational project, are shown in Table II-III. Anti-TNF-alpha treatment, according to ASAS recommendations, could be considered in case 2, 3, 6, 8 and 9. The rheumatologists had an excellent initial agreement with this treatment option with a further significant improvement after the educational program. In case 2, axial SpA with acute anterior uveitis (AU) and in case 8, AS with Crohn's disease, anti-TNF-alpha treatment was indicated mainly as monoclonal anti-TNF antibody; furthermore in case 2, at the end of the project, there was a reduction of the agreement for the option of recombinant fusion protein of human soluble TNF-alpha receptor. In the other cases (case 1, 4, 5, 7 and 10) anti-TNF-alpha treatment according to ASAS recommendations could not be considered. In case 1, 4 and 5 the rheumatologists agreed that anti-TNF-alpha treatment was not suitable, but in case 7 (AS with elevated levels of CRP and poor response to NSAIDs) and 10 (axial SpA with acute AU) this option has been considered useful.

At baseline, in AS cases, there was an excellent agreement to use physical therapy (with supervised exercises, normal or water based, individually or in a group), while in axial SpA cases the agreement was moderate/substantial. Nevertheless, in this group of patients the agreement was excellent (case 1, 2, 4, 5) or substantial (case 3) after the educational programme.

Treatment options with sulfasalazine, methotrexate, systemic glucocorticoids (low or high doses) or corticosteroid injections of sacroiliac joints were not considered an useful approach by rheumatologists involved in this project (poor agreement in all cases).

NSAIDs as first-line drugs could be considered in case 1, 4, 7, 10. The rheumatologists had a preference for a regimen of at least two NSAIDs over a 4-week period in total at maximum recommended dose unless contraindicated

Table I. Adherence to ASAS classification criteria for axial SpA: comparison before and after the educational project (level of agreement 0–10; the values are expressed as median / 25^{th}–75^{th} percentile).

Case	Correct diagnosis	ASAS criteria for axial SpA			modified NY criteria for AS		
		Before the project Level of agreement (0-10)	After the project Level of agreement (0-10)	*p*-value	Before the project Level of agreement (0-10)	After the project Level of agreement (0-10)	*p*-value
1	Axial SpA ASAS criteria	9 (8-9)	10 (10-10)	0.0001	3 (0-7.5)	0 (0-1)	0.003
2	Axial SpA ASAS criteria	8 (5-9)	10 (10-10)	0.0001	2 (0-5)	0 (0-0)	0.003
3	Axial SpA ASAS criteria	8 (0-8)	10 (0-10)	0.0491	3 (0-5.5)	0 (0-0)	0.0001
4	Axial SpA ASAS & NY criteria	9 (8-10)	10 (9-10)	NS	9 (8-10)	10 (10-10)	0.0002
5	Axial SpA-ASAS criteria	8 (5.5-9)	10 (0-10)	NS	5 (0-7.5)	0 (0-8.5)	NS
6	Spine osteoarthritis	0 (0-1)	0 (0-0)	NS	0 (0-1)	0 (0-0)	NS
7	DISH	0 (0-0.5)	0 (0-0)	NS	0 (0-0)	0 (0-0)	NS
8	Facet joints arthrosis	0 (0-0)	0 (0-0)	0.0407	0 (0-0)	0 (0-0)	NS
9	infective disciitis	0 (0-0)	0 (0-0)	0.0459	0 (0-0)	0 (0-0)	NS
10	lumbar disc herniation	1 (5.5)	0 (0-8)	NS	0 (0-1)	0 (0-0)	NS

Table II. Treatment options in non-radiographic axial SpA (case 1–4) and undifferentiated SpA (case 5): comparison before and after the educational project (level of agreement 0–10; the values are expressed as median / 25th–75th percentile).

Treatment Options	*Case 1* IBP, SI (MRI), BASDAI<4, CRP neg, HLA B27 pos		*Case 2* IBP, SI (MRI), BASDAI>4, CRP neg, HLA B27 neg, acute AU		*Case 3* IBP, SI (MRI), BASDAI>4, CRP neg, HLA B27 neg, NSAIDs=LR		*Case 4* IBP, BASDAI<4, CRP neg, HLA B27 neg, SpA family history		*Case 5* IBP, Spine BME, BASDAI<4, CRP neg, HLA B27 neg, NSAIDs=LR	
	before	after	before	after	before	after	before	after	before	after
1	5/0-8	0/0-5.5[b]	0/0-4	0/0-1	0/0-1	0/0-0	1/0-5.5	0/0-6	0/0-4.5	0/0-4
2	9/2-10	10/10-10[d]	6/3.5-10	7/0-10	5/0-9	0/0-9	8/3-10	10/9-10[d]	7/3.5-9	7/2-9
3	0/0-0	0/0-0	0/0-2	0/0-0	0/0-0	0/0-0	0/0-1	0/0-0	0/0-2.5	0/0-0
4	0/0-2	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
5	0/0-1	0/0-0	0/0-2	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
6	5/2.5-10	10/0.5-10	5/0-9	8/0-10	6/0-9	7/0-10	8/3.5-10	10/7-10[b]	9/0-10	10/8-10
7	0/0-5	0/0-0[b]	0/0-5	0/0-0[a]	0/0-6.5	0/0-0[c]	0/0-6.5	0/0-0[c]	0/0-8	0/0-0[c]
8	0/0-0.5	0/0-0	0/0-2.5	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
9	0/0-1.5	0/0-7	0/0- 6.5	0/0-0[c]	6/0-8	9/0-10[a]	0/0-5	0/0-0[a]	0/0-0	0/0-0
10	0/0-5	0/0-7	8/2.5-9.5	10/8-10[b]	8/2-10	10/9-10[d]	0/0-6	0/0-0[c]	0/0-2	0/0-2

SI: sacroiilitis; AU: anterior uveitis; LR: lack of response; BME: bone marrow oedema. [a]$p<0.05$; [b]$p<0.01$; [c]$p<0.001$; [d]$p<0.0001$.
1 at least two NSAIDs for at least 3 months at maximum recommended dose unless contraindicated;
2 at least two NSAIDs over a 4-week period in total at maximum recommended dose unless contraindicated;
3 systemic glucocorticoids (prednisone <10 mg/daily);
4 corticosteroid injections of sacroiliac joints;
5 short (2–3 weeks) treatment with systemic glucocorticoids (prednisone ≥10 to 25 mg/daily);
6 physical therapy with supervised exercises, land or water based, individually or in a group;
7 sulfasalazine (2–3 gr/daily);
8 methotrexate (up to 15–20 mg/weekly);
9 recombinant fusion protein of human soluble TNF-alpha receptor;
10 monoclonal anti-TNF-alpha antibody.

Table III. Treatment options in radiographic axial SpA (case 6–10): comparison before and after the educational project (level of agreement 0–10; the values are expressed as median / 25th–75th percentile).

Treatment options	*Case 6* IBP, SI (Rx), BASDAI> 4, CRP pos, HLA B27 pos, NSAIDs=LR		*Case 7* IBP, SI (Rx), BASDAI<4, CRP pos, HLA B27 neg, NSAIDs=LR		*Case 8* IBP, SI (Rx-MRI), BASDAI>4, CRP pos, HLA B27 pos, Crohn's disease		*Case 9* IBP, SI (Rx-MRI), BASDAI>4, CRP pos, HLA B27 pos, NSAIDs=LR		*Case 10* IBP, SI (Rx), BASDAI<4, CRP neg, CRP neg, HLA B27 pos, acute AU	
	before	after	before	after	before	after	before	after	before	after
1	0/0-2	0/0-2	0/0-1	0/0-0	0/0-0	0/0-0	0/0-2	0/0-0	0/0-2	0/0-0
2	7/0-9.5	5/0-9	6/0-8.5	7/0-10	0/0-5	0/0-7	4/0-7.5	0/0-5.5	5/0-9	4/0-10
3	0/0-0	0/0-0	0/0-0	0/0-0	0/0-5	0/0-0	0/0-1	0/0-0[a]	0/0-0	0/0-0
4	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
5	0/0-0	0/0-0	0/0-1	0/0-0	0/0-0.5	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
6	9/5.5-10	10/6-10	9/5-10	10/5.5-10	9/5-10	10/0-10	8/5-10	10/6-10	9/6-10	10/6.5-10
7	0/0-2.5	0/0-0[a]	0/0-3	0/0-0[a]	0/3-7.5	0/0-0[c]	0/0-2	0/0-0	0/0-0	0/0-0[a]
8	0/0-0	0/0-0	0/0-1	0/0-0	0/0-1	0/0-0	0/0-0	0/0-0	0/0-0	0/0-0
9	6/0-8.5	9/8-10[d]	5/0-8	8/0-10	0/0-6	0/0-9.5	7/3-9	10/8-10[d]	2/0-6.5	0/0-2
10	10/7.5-10	10/9-10	9/6-10	8/0-10[a]	10/8-10	10/10-10[b]	9/8-10	10/10-10	9/6.5-10	10/8-10

SI: sacroiilitis; AU: anterior uveitis; LR: lack of response. [a]$p<0.05$; [b]$p<0.025$; [c]$p<0.0001$; [d]$p<0.0005$.
1 at least two NSAIDs for at least 3 months at maximum recommended dose unless contraindicated;
2 at least two NSAIDs over a 4-week period in total at maximum recommended dose unless contraindicated;
3 systemic glucocorticoids (prednisone <10 mg/daily);
4 corticosteroid injections of sacroiliac joints;
5 short (2–3 weeks) treatment with systemic glucocorticoids (prednisone ≥10 to 25 mg/daily);
6 physical therapy with supervised exercises, land or water based, individually or in a group;
7 sulfasalazine (2–3 gr/daily);
8 methotrexate (up to 15–20 mg/weekly);
9 recombinant fusion protein of human soluble TNF-alpha receptor;
10 monoclonal anti-TNF-alpha antibody.

drug treatment according to recommendations for the management and for the use of anti-TNF-alpha in AS/axialSpA. The agreement ranged from moderate to excellent.

Discussion

ASAS classification criteria define axial SpA if a patient has a chronic back pain (>3 months) and age at onset less than 45 years, in the presence of sacroiliitis by radiography or by magnetic resonance imaging (MRI) plus at least one SpA feature (''imaging arm'') or the presence of HLA-B27 plus at least two SpA features (''clinical arm'') (3). These criteria permit to include in the same spectrum of disease patients with AS according to NY modified criteria (4) and patients without definite radiographic sacroiliitis, also referred to as non-radiographic axial SpA. In the specific setting of the rheumatology referral centres who developed these criteria, the diagnostic performance for axial SpA has been considered good. In fact, the disease probability of SpA was 89.0% or 23.5% if these criteria were fulfilled or not fulfilled (3). In the present study we determined the adherence of practicing rheumatologists, to ASAS classification criteria for axial SpA, both before and after an educational project. In five (four non-radiographic) axial SpA cases, examined for diagnostic purpose, the rheumatologists had an excellent agreement with ASAS classification criteria for axial SpA, both before and after the educational project. However, the training course led to an improvement of level of agreement, which was statistically significant for some cases. This result is interesting because the diagnosis of non-radiographic axial SpA, might be difficult in some cases, especially when there is a lack of collaboration between rheumatologist and radiologist to search bone marrow oedema/osteitis. The adherence to these criteria was also confirmed by the evidence of a poor agreement in the remaining non-axial SpA cases.

The adherence of practicing rheumatologists to the ASAS criteria for axial SpA is the first step toward the use of TNF-alpha blockers in the non-radiographic stage of this condition. In this study, we also determined the adherence of the rheumatologists involved in the educational project to ASAS recommendations for the use of anti-TNF-alpha agents in patients with axial SpA (7). These recommendations, which take into account the new axial SpA criteria (7), are incorporated into the ASAS/EULAR recommendations for the management of AS (8). In ten axial SpA cases examined for therapeutic purpose, practicing rheumatologists generally showed an excellent agreement with the choice of starting or not starting anti-TNF-alpha treatment according to ASAS recommendations. The presence of extra-articular manifestations (*i.e.* Crohn's disease) led to the choice of a monoclonal anti-TNF-alpha antibody instead of the recombinant fusion protein of human soluble TNF-alpha receptor. These results are consistent with ASAS recommendation n. 9 on anti-TNF-alpha therapy (8), which states that "there is no evidence to support a difference in efficacy of the various TNF inhibitors on the axial and articular/entheseal disease manifestations; but in the presence of IBD (inflammatory bowel disease) difference in gastrointestinal efficacy needs to be taken into account" (8). This statement is supported by evidence showing a significantly lower incidence rates of IBD during treatment with infliximab, as compared with etanercept or adalimumab (14) and efficacy and safety of adalimumab in inducing and maintaining clinical remission in patients with moderate-to-severe ulcerative colitis (15, 16) and with moderate to severe Crohn's disease (17, 18). In our study, the clinical impact of extra-articular manifestations on the management of axial SpA/AS was additionally showed by case 2 and 10. According to ASAS recommendations, anti-TNF-alpha treatment should not be considered in case n.10, but the presence of acute AU, as well as in case n. 2, conditioned the choice for a monoclonal anti-TNF antibody. An update of the literature review on treatment with biologics; reported that acute AU was less frequent during anti-TNF treatment, respect to placebo (19). The incidence rates/100 patient-years of AU during infliximab, etanercept or placebo was 4.4 ($p<0.005$), 7.9 ($p<0.05$) or 15.6, respectively (20). Another study showed that the incidence of AU flares under open-label adalimumab treatment was lower than the incidence rate of AU during the previously performed placebo-controlled period of the same trial (7.4 vs 15.0 AU flares/100 patient-years ($p=0.001$) (21). A significant decrease (73%) in the recurrence rate of AU during adalimumab treatment was reported in patients with AS (22). These data support the choice of the rheumatologists that considered anti-TNF-alpha treatment, mainly monoclonal antibody, in cases with refractory uveitis or a high uveitis recurrence rate, even if ASAS recommendations for the use of anti-TNF-alpha agents in patients with axial SpA were not fulfilled.

In case 1, 4 and 5 the rheumatologists agreed that anti-TNF-alpha treatment was not suitable, but in case 7 this option has been considered useful. Despite the low BASDAI, in this patient the elevated levels of C-reactive protein (CRP) and worsening of function, were probably the reasons for this choice. CRP represents an useful tool to assess disease activity as demonstrated by its inclusion in the AS Disease Activity Score (ASDAS) (23). Moreover, elevated CRP levels have shown to be a positive predictor of radiological progression (24) and outcome to anti-TNF-alpha treatment in randomised or observational studies (25, 26). Actually, previous studies underlined that rheumatologists considered both disease activity and severity to be determinants of starting TNF blockers, even if their decision could be in disagreement with ASAS recommendations (9-11).

After the educational program there was an excellent agreement in all patients (except case n. 3) to use physical therapy (with supervised exercises, land or water based, individually or in a group) with or without anti-TNF-alpha treatment. These results are consistent with the statement that the cornerstone of non-pharmacological treatment of patients with AS is patient education and regular exercise (8), and the clinical experiences showing that a combination approach with non-pharmaco-

logical treatment and anti-TNF-alpha agents was beneficial for patients with AS, with synergistic effects on pain, function and disability (27-29).

Treatment options with sulfasalazine, methotrexate, systemic glucocorticoids (low or high doses) were not considered by the rheumatologists involved in this project (poor agreement in all cases), according to the lack of evidence on the use of these drugs for axial disease (8). Corticosteroid injections of sacroiliac joints were also not considered probably because of real-life difficulties to perform computed tomography or ultrasound-guided injections.

Among treatment options, NSAIDs as first-line drug treatment according to the recommendations for the management and for the use of anti-TNF-alpha in AS/axialSpA were considered important. The rheumatologists had a preference for a regimen of at least two NSAIDs over a 4-week period in total at maximum recommended dose unless contraindicated. This agreement, which ranged from moderate to excellent, suggests that also practicing rheumatologists shared the decision of ASAS members that this approach prevents a patient continuing with an ineffective NSAID and having the risk of adverse events without a possible benefit (7).

In conclusion, our study showed that practicing rheumatologists had a satisfying adherence to ASAS classification criteria and to ASAS recommendations for the use of anti-TNF-alpha agents for patients with axial SpA. However, the educational project further improved this adherence. In addition, this study confirms that extra-articular manifestations and other variables might play a role in the decision-process of the management of axial SpA, suggesting the need for continued exchange among the medical community to increase sharing of the ASAS recommendation.

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