Prediction of Work Impact in Axial Spondyloarthritis by the Work Instability Scale: A Prospective Cohort Study of 101 Patients

Irina Cucos, Sabrina Dadoun, Charlotte Jacquemin, Sarah Kreis, Stephanie Fabre, Christophe Hudry, Eduard Pertuiset, Bruno Fautrel, Laure Gossec

Prediction of work impact in axial spondylarthritis by the Work instability Scale, a prospective cohort study of 101 patients.

Irina Cucos, 0000-0003-0785-6074, Sabrina Dadoun, Charlotte Jacquemin 0000-0002-2826-9605, Sarah Kreis, Stephanie Fabre, Christophe Hudry , Eduard Pertuiset, Bruno Fautrel 0000-0001-8845-4274, Laure Gossec, 0000-0002-4528-310X

Name of department(s) and institution(s) to which the work should be attributed : Rheumatology Department, Pitié-Salpêtrière Hospital, AP-HP, Paris, France

I. Cucos MD (1), S. Dadoun MD (2), C. Jacquemin MD (3,4), S. Kreis MD (3), S. Fabre MD (3), C. Hudry MD (2), E. Pertuiset PhD (4), B. Fautrel PhD (1,3), L. Gossec PhD (1,3).

1. Rheumatology Department, Pitié-Salpêtrière Hospital, AP-HP, Paris, France.
2. Private practice, Paris, France
3. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France.
4. Rheumatology department, Rene Dubos Hospital, Pontoise, France

CORRESPONDING AUTHOR
Irina Cucos,
Saint Mary Clincial Hospital, Rheumatology Department, 37-39, Ion

Mihalache, Bucharest, 011172, Romania

Irina.cucos@yahoo.com

Running head: AS-WIS predicts work impact

Abstract (241 words, limit 250)

Introduction: Axial spondyloarthritis (axSpA) may have an impact on work. The Ankylosing Spondylitis Work Instability Scale (AS-WIS) assesses difficulties at work. The objective of this study was to evaluate the predictive value of the AS WIS on work impact.

Patients and methods: Prospective cohort study with two timepoints (at baseline and after 1.5 years) including patients with axSpA and a paid professional activity. Patients completed the AS-WIS at baseline and work instability was scored as moderate/high if ≥11 (0-20 scale). At follow up, adverse work outcomes (AWO) were defined as short-term sick leave or severe AWO (long-term sick leave, disability, unemployment). Univariable and multivariable logistic regression analyses were performed to explain AWO.

Results: Of 101 patients, mean age 45 (standard deviation (SD) 9) years, 52% male, disease duration was 14 (SD 8) years. The BASDAI and the BASFI were respectively 34 (SD 21) and 23 (SD 23), 69 (68%) received a TNF-inhibitor. At baseline, 46 (46%) patients had moderate/high AS-WIS. At 1.5 years of follow-up, 37 patients (36%) had AWO: 25 patients (25%) a short-term sick leave, and 12 patients (12%, 7/100 patient years) a severe AWO. Independent baseline factors associated with AWO were a moderate/high AS-WIS score (odds ratio 2.71 [95% confidence interval 1.04-7.22]) and shorter disease duration (0.94 [0.89-0.99]).

Conclusion: In patients with axSpA, a moderate/high AS-WIS score was predictive of AWO in this population with well-controlled axSpA. This short questionnaire can be helpful to screen for future difficulties at work.

Introduction

Axial spondyloarthritis (axSpA) affects the working age subject and has an important impact on the patients' ability to work. Studies showed that work impact for patients with spondyloarthritis ranges from 22% to 31%(1–3) depending on the definition used for work disability, from reducing working hours, to short term or long term sick leave, or loss of work and unemployment. The risk of unemployment was 5% in the first year, and 31% at 20 years of disease.(3) Loss of employment is associated with socioeconomic factors, comorbidities, disease status (disease duration, greater physical impairment and pain) and psychological distress (anxiety, depression)(4,5).

Understanding the importance of the disease's impact on the patient's working capacity may be useful in order to develop preventive measures and adaptation of the work conditions. An objective tool to evaluate difficulties at work is the Ankylosing Spondylitis Work Instability Scale (AS-WIS), a 20-item questionnaire developed in 2009, which identifies patients thought to be at low (<11 points), moderate (11-18 points) or high (>18 points) risk of work instability(6). The initial study included 57 patients, of whom 40% had moderate to high levels of work instability.(6) Other authors have confirmed the feasibility of the AS-WIS(7).

However, to date no study has assessed the predictive value of the AS-WIS. This has been assessed in rheumatoid arthritis, using the Rheumatoid Arthritis Work Instability Scale(8), which was found useful to predict adverse work outcomes (AWO) at 1 year of follow up.(9)

Thus, the main objective of this study was to evaluate the predictive value of the AS-WIS on work impact of ax SpA.

Patients and Methods

Participants and study design

This was a prospective cohort study with two timepoints (at baseline and after

4

1.5 years) in 3 centers in Paris, France. The baseline data regarding other aspects of this study have been previously published (7,10–12). All patients with axSpA according to the rheumatologist and the ASAS classification criteria (13) seen in hospitalization or outpatient clinic, between September 2013 and February 2014 were contacted by mail and sent a questionnaire. The baseline questionnaire was sent to 240 patients.

For patients who had answered the baseline questionnaire and were currently in a paid work position, a second questionnaire was sent after 1 year with 2 subsequent reminders if needed, at 6 and 12 months.

Work instability

The AS-WIS questionnaire was used to assess the impact of the disease on work capacity. The AS-WIS had been previously translated, cross-culturally adapted and validated in French (8). It is a 20-item simple screening tool for work instability (the consequences of a mis-match between an individual's functional ability and their work tasks)(8). The AS-WIS varies between 0 and 20 with higher numbers indicating higher instability; it was scored here as proposed by the scale's authors, as low if the score was <11, moderate between 11-18 and high >18(6).

AWO

At follow-up, four different events were defined as AWO: short term sick leave (<3 months), long term sick leave (between 3 months and 2 years) , work disability (state-accepted status of incapacity to work) and unemployment (corresponding here to loss of employment). They were grouped into moderate AWO (short term sick leave) and severe AWO (long term sick leave, disability and unemployment).

Data collection at baseline

Demographic characteristics including age, gender, body mass index, education level, and work status (employed, unemployed or unable to work) were collected. Also, the patients were asked to answer the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)(14) and Bath Ankylosing Spondylitis Functional Index (BASFI)(15). The medical files were accessed to

obtain data on the presence of HLA-B27, radiographic sacroiliitis and presence of high CRP.

Statistical analysis

Statistical analysis included descriptive analyses of AWO, AWO per 100 patient years and AS-WIS scores. Variables analysed in the univariable analysis included demographic data, type of work, level of studies and disease-related variables (BASDAI, BASFI, current TNF-blocker treatment, radiographic sacroiliitis and HLA B27). Variables with a p value below 0.10 in univariable analysis were further tested in multivariable analysis, without any other selection criteria. An exploratory analysis of predictors of severe AWO was also run. There was no imputation of missing data.

Ethics and consent

This study was approved by the Pitie-Salpetriere Ethics Committee (2014_04) and patients signed an informed consent.

Results

Patients' description

Among the 209 patients who answered the first questionnaire, 144 were currently working and 101 (70% of 144) answered the second questionnaire. Among patients not working, most were retired (12%) or in work disability/long-term sick leave (9%). Those 43 who did not answer the second questionnaire had similar demographic characteristics to the responders (data not shown). Mean age at inclusion was 45 (standard deviation SD 9) years, 52 (52%) were male, disease duration was 14 (SD 8) years and 62 (62%) had an education level equivalent to more than high school. More patients had white-collar jobs (N=59, 58% of available data) than blue-collar jobs (N=26, 25%), The BASDAI and the BASFI were respectively 34 (SD 21) and 23 (SD 23). At baseline, 69 (68%) received a TNF-inhibitor treatment (table 1).

AS-WIS at baseline

The mean AS-WIS (0-20 scale) was 9 (standard deviation, SD 5) with a median of 10, a low-risk score was found in 55 patients (54%), and a moderate/high risk score in 46 (46%) (figure 1). The questions that were most often scored as present in the ASWIS referred to the relationship between pain and patients' ability to concentrate on tasks (question 4, 79% positive answers) and to variability across days (bad days/good days, question 9, 77%).

AWO

The mean (SD) follow up was 1.5 (0.3) years. At follow up, 37 patients (36%) had AWO: 25 patients (25%) a short-term sick leave, and 12 patients (12%) severe AWO (4 (4%) long term sick leave, 5 (5%) disability, 3 (3%) unemployment). All patients who reported loss of employment stated that the cause was SpA-related.

Overall, 17 (16%) patients had to adapt their work place, 6 (6%) had to change their work place without changing profession, 1(1%) had to change profession and 2 patients (2%) switched from full time to half time. Out of 46 patients with moderate/high AS-WIS, 11(24%) of patients had to adapt their work place, 2 (4%) of patients changed workplace and one patient (2%) changed profession. No patient in this group reduced the working hours.

Over the follow up of 159 patient-years, the rate of any AWO was 23/100 patient-years and of severe AWO was 7/100 patient-years.

Predictors of AWO

In univariable analysis (table 2), baseline factors associated with any AWO were a moderate/high AS-WIS score, a high BASFI and a shorter disease duration. Apart from the BASFI, no other disease-related variables were significant. In multivariable analysis, moderate/high AS-WIS (odds ratio, OR 2.71 [95% confidence interval 1.04-7.22]) and lower disease duration (OR: 0.94 [0.89-0.99]) were independent predictive factors of AWO. Of note, a moderate/high AS-WIS score was not predictive of severe AWO, but severe AWO were rare (N=12).

Among patients with a low AS-WIS score at baseline (n=55), only 13 (24%)

had AWO (including only 2 (3%) with severe AWO). Among patients with a moderate/high AS-WIS score (n=46), 24 (52%) had AWO (including 10 (21%) patients with severe AWO) (figure 2).

Discussion

In the present study, we demonstrated the predictive value of the AS-WIS for work impact in axSpA over a follow up of 1.5 years. We found that the risk of AWO was relatively frequent in this population of stabilized axSpA patients, with 37 (36%) patient with AWO and 12 patients (7/100 patient-years) with severe AWO. Furthermore, the risk of AWO was almost trebled by a moderate/high work instability risk, as assessed by the AS-WIS. The use of the AS-WIS might allow targeted interventions for work maintenance.

This study has a number of limits. The number of patients is relatively small and the duration of the follow up is moderate(1). However, the study validating the RA-WIS in rheumatoid arthritis had a similar size and duration of follow up(9) and our study did not lack power. There was no confirmation of the AWO (by physician or social insurance), we used patient-reported data. However, patient-reported outcomes are usually found to be reliable(16). It is possible that not all variables of interest (such as potential effect modifiers) were taken into account in the analyses. AWO and in particular loss of work is of course multi-factorial, with elements related to soci-economic factors on top of disease-related causes. In the present study we did not collect enough non-disease-related variables to be able to fully assess this point. We chose to pool all AWO in the present study. It can be discussed that short term sick leave is not relevant for work instability, but it was previously shown that prior sick leave predicts future AWO (17,18). Therefore, head-to-head comparisons are difficult to make, since definitions of AWO included in these studies are different (some of the studies don't include short-term sick leave). Also, a time-to-event analysis might have brought additional information. The study dates from 2014, which may be considered a weakness, since the management options in axSpA have evolved (19). However, our study included patients form a tertiary care center, with a high rate of biologics

being used. Thus, we believe the present results are relevant.

The high rate of patients experiencing AWO confirms the impact of axSpA on employement status. Previous studies have found a prevalence of AWO of 22% for a followup of 12 years(1), a lower rate than in our study. These results are surprising, considering the fact that we included a more recent cohort, with a higher proportion of patients treated by biologic therapy (68% vs 14% in OASIS(1)). The high number of patients treated by biologics suggests that this is a cohort of patients who may have had very active disease though activity at the time of study was low and severity was moderate (as indicated by 21% patients with syndesmophytes). The high activity of the disease at some point in time may explain the higher percentage of AWO.There are, of course differences between countries' health insurance systems, and it was recently shown that higher country healtcare expediture is associated with higher job maintenance(20). Another factor to be considered could be the psychological profile of the patients, which could have changed over recent years due to shifts in expectations(21–24).

When exploring severe AWO, we found that only 12% of our patients, i.e., 7/100 patient years experienced severe work impact, of whom 3 (3%) were unemployed, a much lower finding than what was previously reported in the literature (around 20%)(2). This could be due to the fact that our study included only patients with paid work, leading to a skewed distribution in this population. An inception cohort would allow to describe AWO taking into account the natural history of the disease, however to date no such studies are available(25).

The main predictors for AWO in our study were moderate/high AS-WIS at baseline and shorter disease duration. The latter could be explained by the skewed nature of our population since to be included, patients were by definition not in work disability. Thus patients with long-standing disease may have already experienced AWO (left-censoring).

The risk of experiencing AWO at 1.5 years of follow up was increased almost

three-fold for patients with moderate/high AS-WIS scores. This suggests that a score>11 could raise concerns for the sustainability of a patient's current work status. Interestingly, neither the functional capacity nor the disease activity proved to be predictive for AWOwhich is in contradiction to previous studies(7) (18,26,27), potentially due to the skewed nature of our population. In this well stabilized and biologic-treated cohort, it is interesting to note a rate of 7/100 patient years for severe AWO. We consider that patient information on this finding is important and should lead to adaptation of job conditions if necessary, but also to shared decision-making in terms of treatment. Targeted interventions for work maintenance can include psychological support for patients who score high in the anxiety, fatigue or burden of the disease questions,and/or pain management, for patients who score high on pain-related questions.

In conclusion, we have demonstrated the predictive value of the AS-WIS for AWO; the use of this score in daily practice to identify patients at risk of AWO should be further explored with the objective to facilitate work retention in our patients.

References

1. Castillo-Ortiz JD, Ramiro S, Landewé R, Van Der Heijde D, Dougados M, Van Den Bosch F, et al. Work Outcome in Patients with Ankylosing Spondylitis: Results from a 12-Year Followup of an International Study. Arthritis Care Res. 2016;68:544–62.

2. Montacer Kchir M, Mehdi Ghannouchi M, Hamdi W, Azzouz D, Kochbati S, Saadellaoui K, et al. Impact of the ankylosing spondylitis on the professional activity. Joint Bone Spine. 2009;76:378–82.

3. Boonen A, Chorus A, Miedema H, Van der Heijde D, Landewé R, Schouten H, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. Ann Rheum Dis. 2001;60:1033–9.

4. Barlow JH, Wright CC, Williams B, Keat A. Work disability among people with ankylosing spondylitis. Arthritis Rheum. 2001 Oct;45:424–9.

5. Nikiphorou E, Ramiro S, van der Heijde D, Norton S, Moltó A, Dougados M, et al. Association of Comorbidities in Spondyloarthritis With Poor Function, Work Disability, and Quality of Life: Results From the Assessment of SpondyloArthritis International Society Comorbidities in Spondyloarthritis Study. Arthritis Care Res. 2018;70:1257–62.

6. Gilworth G, Emery P, Barkham N, Smyth MG, Helliwell P, Tennant A. Reducing work disability in Ankylosing Spondylitis - Development of a work instability scale for AS. BMC Musculoskelet Disord. 2009;10.

7. Fabreguet I, Koumakis E, Burki V, Durnez A, Elhai M, Meyer M, et al. Assessment of work instability in spondyloarthritis: A cross-sectional study using the ankylosing spondylitis work instability scale. Rheumatology. 2012;51:333–7.

8. Gilworth G, Chamberlain MA, Harvey A, Woodhouse A, Smith J, Smyth MG, et al. Development of a work instability scale for rheumatoid arthritis. Arthritis Rheum. 2003;49:349–54.

9. Tang K, Beaton DE, Gignac MAM, Lacaille D, Zhang W, Bombardier C. The Work Instability Scale for rheumatoid arthritis predicts arthritis-related work transitions within 12 months. Arthritis Care Res. 2010;62:1578–87.

10. Kreis S, Molto A, Bailly F, Dadoun S, Fabre S, Rein C, et al. Relationship between optimism and quality of life in patients with two chronic rheumatic diseases: axial spondyloarthritis and chronic low back pain: a cross sectional study of 288 patients. Health Qual Life Outcomes. 2015;13:78.

11. Fabre S, Molto A, Dadoun S, Rein C, Hudry C, Kreis S, et al. Physical activity in patients with axial spondyloarthritis: a cross-sectional study of 203 patients. Rheumatol Int. 2016;36:1711–8.

12. Fabre S, Molto A, Kreis S, Hudry C, Fautrel B, Pertuiset E, et al. Is the widely-used score in axial spondyloarthritis, Bath Ankylosing Spondylitis Disease Activity Index, influenced by patients' optimism? A cross-sectional study of 206 patients. Joint Bone Spine. 2017;84:629–30.

13. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. 2009;68:777–83.

14. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994, 21:2286–91.

15. Calin A, Jones SD, Garrett SL, Kennedy LG. Bath Ankylosing Spondylitis Functional Index. Br J Rheumatol. 1995;34:793–4.

16. Fautrel B, Alten R, Kirkham B, de la Torre I, Durand F, Barry J, et al. Call for action: how to improve use of patient-reported outcomes to guide clinical decision making in rheumatoid arthritis, Rheumatology International. Springer Verlag; 2018, 38: 935–47.

17. Webers C, Ramiro S, Landewé R, van der Heijde D, van den Bosch F, Dougados M, et al. Sick leave and its predictors in ankylosing spondylitis: long-term results from the Outcome in Ankylosing Spondylitis International Study. RMD open. 2018 4(2).

18. Macfarlane GJ, Shim J, Jones GT, Walker-Bone K, Pathan E, Dean LE. Identifying persons with axial spondyloarthritis at risk of poor work

outcome: Results from the british society for rheumatology biologics register. J Rheumatol. 2019;46:145–52.

19. Van Der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van Den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76:978–91.

20. Rodrigues Manica S, Sepriano A, Ramiro S, Pimentel Santos F, Putrik P, Nikiphorou E, et al. Work participation in spondyloarthritis across countries: analysis from the ASAS-COMOSPA study. Ann Rheum Dis. 2018;77(9):1303–10.

21. De Wit MPT, Kvien TK, Gossec L. Patient participation as an integral part of patient-reported outcomes development ensures the representation of the patient voice: A case study from the field of rheumatology. RMD Open. 2015 Jan 1;1.

22. Gossec L, Dougados M, Dixon W. Patient-reported outcomes as end points in clinical trials in rheumatoid arthritis, RMD Open; 2015, 1.

23. Putrik P, Ramiro S, Hifinger M, Keszei AP, Hmamouchi I, Dougados M, et al. In wealthier countries, patients perceive worse impact of the disease although they have lower objectively assessed disease activity: results from the cross-sectional COMORA study. Ann Rheum Dis. 2016;75:715–20.

24. Garrido-Cumbrera M, Poddubnyy D, Gossec L, Gálvez-Ruiz D, Bundy C, Mahapatra R, et al. The European Map of Axial Spondyloarthritis: Capturing the Patient Perspective-an Analysis of 2846 Patients Across 13 Countries. Curr Rheumatol Rep. 2019;21:19.

25. Molto A, Tezenas Du Montcel S, Wendling D, Dougados M, Vanier A, Gossec L. Disease activity trajectories in early axial spondyloarthritis: Results from the DESIR cohort. Ann Rheum Dis. 2017;76:1036–41.

26. Ulus Y, Akyol Y, Bilgici A, Kuru O. Association of work instability with fatigue and emotional status in patients with ankylosing spondylitis: comparison with healthy controls. Clin Rheumatol. 2019;38:1017–24.

27. de Hooge M, Ramonda R, Lorenzin M, Frallonardo P, Punzi L, Ortolan A, et al. Work productivity is associated with disease activity and

functional ability in Italian patients with early axial spondyloarthritis: an observational study from the SPACE cohort. Arthritis Res Ther. 2016;18:265.

Figure 1. Legend

X axis: AS-WIS score as baseline by intervals of 2 points

Y axis: number of patients

Figure 2: Legend

X axis: Any AWO vs. severe AWO in patients with low and moderate/high AS-WIS score

Y axis: percentage of patients