A prospective clinical investigation of the effects of anti-TNF alpha therapy on exercise capacity in patients with ankylosing spondylitis

ERHAN ÇAPKIN
SEYHAN BİLGE KESKİN
MURAT KARKUCAK
AHMET AYAR

Follow this and additional works at: https://journals.tubitak.gov.tr/medical
Part of the Medical Sciences Commons

Recommended Citation
ÇAPKIN, ERHAN; KESKİN, SEYHAN BİLGE; KARKUCAK, MURAT; and AYAR, AHMET (2019) "A prospective clinical investigation of the effects of anti-TNF alpha therapy on exercise capacity in patients with ankylosing spondylitis," Turkish Journal of Medical Sciences: Vol. 49: No. 1, Article 5. https://doi.org/10.3906/sag-1805-291
Available at: https://journals.tubitak.gov.tr/medical/vol49/iss1/5

This Article is brought to you for free and open access by TÜBİTAK Academic Journals. It has been accepted for inclusion in Turkish Journal of Medical Sciences by an authorized editor of TÜBİTAK Academic Journals. For more information, please contact academic.publications@tubitak.gov.tr.
A prospective clinical investigation of the effects of anti-TNF alpha therapy on exercise capacity in patients with ankylosing spondylitis

Erhan ÇAPKIN1, Seyhan Bilge KESKİN2, Murat KARKUCAK1, Ahmet AY AR3

1Division of Rheumatology, Department of Physical Medicine and Rehabilitation, School of Medicine, Farabi Hospital, Karadeniz Technical University, Trabzon, Turkey
2Department of Physical Medicine and Rehabilitation, School of Medicine, Farabi Hospital, Karadeniz Technical University, Trabzon, Turkey
3Department of Physiology, School of Medicine, Karadeniz Technical University, Trabzon, Turkey

Background/aim: The purpose of this study was to investigate possible effects of anti-TNF alpha therapy on cardiorespiratory fitness and physical functional capacity of patients with ankylosing spondylitis (AS).

Materials and methods: Twenty-eight AS patients meeting the modified New York criteria with active disease state and an equivalent number of healthy individuals as the control were prospectively enrolled. Physical working capacity and aerobic exercise capacity of the participants were determined by using cardiopulmonary exercise tests, performed before and 4 months after initiation of anti-TNF alpha therapy.

Results: The mean age of the patients was 37 ± 9.1 years, and mean duration of disease was 8.9 ± 7.6 years. Patients with AS exhibited significantly lower aerobic exercise capacity (VO2peak: 21.2 ± 5.5 vs. 27.2 ± 6.6 ml/kg/min, P = 0.001), maximum power output (110.4 ± 34.8 vs. 153 ± 39.8 W, P = 0.0001), and exercise duration (16.3 ± 2.6 vs. 19.6 ± 2.9 min, P = 0.0001) than the healthy controls. When patients were reevaluated after 4 months of anti-TNF alpha therapy, significant improvement was obtained in patients’ aerobic capacity, maximum power output, and exercise duration.

Conclusion: Results from this study indicate that in addition to inflammatory parameters and quality of life index, even short-term anti-TNF alpha therapy results in significant improvement in cardiopulmonary health status as objectively reflected by peak VO2, maximum work rate, and exercise duration.

Key words: Ankylosing spondylitis, anti-TNF alpha therapy, aerobic capacity, physical functional capacity

1. Introduction
Ankylosing spondylitis (AS) is a chronic inflammatory disease involving mainly the sacroiliac joints and the spine (1). AS may show extraarticular manifestations, including cardiovascular and pulmonary involvements (2). In conjunction with systemic inflammation, extraarticular involvement can seriously impair exercise capacity and overall quality of life of patients. Physical functioning in AS is independently determined by both disease activity and radiographic damage of the spine. AS can also lead to significant exercise intolerance (3). AS-associated comorbidities show a significant correlation with the disease activity index (4,5). By investigating the levels of fatigue in patients with AS, Dagfinrud et al. determined significantly more fatigue, with about one out of three reporting serious levels of fatigue, compared with the general population (6). Pain, mobility restrictions, sleep disturbance, and fatigue are among the common problems causing poor quality of life in patients with AS. Thus, given the early age of onset, the chronic and progressive nature of pain, severe deformity, and impairment of life quality and work capacity are serious issues in AS with profound effects on individuals and society on a large scale (7–10). The primary aim of current AS therapy is to relieve symptoms as well as maintain functionality, improve quality of life, and prevent structural damage(s). To achieve these goals, pharmacological and nonpharmacological interventions are utilized in combination. Antitumor necrosis factor (TNF) alpha agents are currently the best medical therapy choice for AS. These agents not only provide improvement
maximum oxygen uptake (VO2max), the highest attainable (12,13). Among the parameters measured during CPET, to medical or surgical therapy or a rehabilitation program the overall health of individuals at baseline and in response exercise performance and functional capacity, and thereby exercise testing, CPET allows objective evaluation of data during maximal symptom-limited incremental blood pressure, and pulse oximetry. By gathering these ventilation (VE) along with electrocardiography (ECG), related to cardiorespiratory function, including oxygen uptake (VO2), carbon dioxide output (VCO2), and minute ventilation (VE) along with electrocardiography (ECG), blood pressure, and pulse oximetry. By gathering these data during maximal symptom-limited incremental exercise testing, CPET allows objective evaluation of exercise performance and functional capacity, and thereby the overall health of individuals at baseline and in response to medical or surgical therapy or a rehabilitation program (12,13). Among the parameters measured during CPET, maximum oxygen uptake (VO2max), the highest attainable rate of transport and use of oxygen by the body during intense exercise, is considered the standard expression of exercise capacity (14).

The aim of this study was to objectively evaluate the cardiorespiratory fitness and physical exercise capacity and response to anti-TNF alpha therapy in patients with AS. The AS patients performed CPET with an incremental ramp protocol to the limit of tolerance before and 4 months after starting anti-TNF therapy.

2. Materials and methods
Twenty-eight patients with active AS (BASDAI score of 4 or above) meeting the modified New York diagnostic criteria, with no peripheral joint involvement, aged 18–50 years and who had not previously received anti-TNF alpha therapy, were enrolled in the study. Patients were assessed in terms of the study parameters before anti-TNF alpha therapy and 4 months after commencing therapy. An equivalent number of healthy individuals matched in terms of age, sex, body mass index (BMI), and smoking status were enrolled as the control group. Voluntary consent forms were obtained from the patient and control groups. Patients with exercise intolerance, heart or lung disease, or peripheral joint involvement were excluded. Approval for the study was granted by the Karadeniz Technical University Medical Faculty Local Ethical Committee.

2.1. Evaluation parameters
Patients’ age, sex, BMI, smoking status, duration of disease, delay in diagnosis, and length of drug use were recorded. Evaluation of the patient group before treatment and at the 4th month of treatment and that of the control group was performed by the same clinician (SBK). Chest expansion, the Bath Ankylosing Spondylitis Metrology Index (BASMI), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), and the Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) were used. Routine full blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) values were measured concomitantly with clinical evaluation.

2.2. Respiratory function test (RFT)
RFTs were performed using a Koko Legend ergospirometer. The device was recalibrated before each test. Calibration was regarded as valid when a margin of error of less than 3% had been established, as recommend by the American Thoracic Association. The temperature and humidity in the room where the exercise test was performed were adjusted to the weather conditions. Patients were given a detailed explanation of the respiratory maneuvers they would need to perform during the RFT, and dynamic tests were then performed. Forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC values were thus determined. Measurements were repeated so that the difference between three tests should be less than 10%, and the best value automatically determined by the computer was recorded.

2.3. Cardiopulmonary exercise test (CPET)
Maximum oxygen consumption (VO2max) is widely regarded as the scale that best indicates cardiovascular performance and aerobic exercise capacity. During exercise, oxygen consumption (VO2) rises in parallel with work load until a plateau is reached. This plateau represents the point at which VO2 (mL/kg per min or L/ min) will rise no further despite an increasing work load and shows the individual’s VO2max (or aerobic capacity) value. Measurement of VO2 is very useful in objectively identifying the physical work performed by an individual. The main factors affecting VO2max are age, sex, exercise habits, and cardiac status. Women have less muscle mass, lower hemoglobin levels, and lower blood volume and cardiac output than men, and their VO2max values are lower in association with these factors. VO2max will be high in individuals with high physical activity levels.

All exercise tests were performed in the morning hours (0900–1100 hours), immediately after diagnosis of
active disease state and 4 months after initiation of anti-TNF alpha therapy. On the exercise test day, patients were advised to dress comfortably, not to eat or smoke for 3 h beforehand, to drink water so as to ensure normal hydration, to avoid any excessively tiring exercise apart from routine activity, and to sleep for 6 h the night before the test (12). A bicycle ergometer, the most commonly employed modality, was used for the exercise test. The test was performed for every volunteer using bicycle ergometry with a gradually increasing work rate (loading test). The exercise test, in which work rate is gradually increased, began with a warm-up period of 5 min at a work rate of 20 W. At the end of the warm-up period, the work rate was increased by 15 W a minute (5 W/20 s) in a computer-controlled manner. The increase varies according to the health status of the individual and was maintained until each subject could no longer rotate the pedals (not falling below 40 rpm), or in other words until the patient’s ‘exercise potential’ with maximum effort was exhausted. Individuals’ maximal effort capacities (W max, watts) and ‘exercise potential’ with maximum effort was exhausted. falling below 40 rpm), or in other words until the patient’s health status of the individual and was maintained

The increase varies according to the health status of the individual and was maintained until each subject could no longer rotate the pedals (not falling below 40 rpm), or in other words until the patient’s ‘exercise potential’ with maximum effort was exhausted. 

Individuals’ maximal effort capacities (W max, watts) and ‘exercise potential’ with maximum effort was exhausted. falling below 40 rpm), or in other words until the patient’s

was increased by 15 W a minute (5 W/20 s) in a computer-controlled manner. The increase varies according to

the health status of the individual and was maintained until each subject could no longer rotate the pedals (not falling below 40 rpm), or in other words until the patient’s ‘exercise potential’ with maximum effort was exhausted.

Individuals’ maximal effort capacities (W max, watts) and ‘exercise potential’ with maximum effort was exhausted. falling below 40 rpm), or in other words until the patient’s ‘exercise potential’ with maximum effort was exhausted.
based on responses of organs at physiological functional limits, not just at rest, by providing submaximal and peak exercise responses. Since CPET provides objective data concerning physiological functional capacity and losses occurring in that capacity due to diseases, and about improvements caused by therapeutic interventions (medical, surgery, and physiotherapy), it is being used in an increasingly broad clinical spectrum (12). Examination of oxygen consumption ($\text{VO}_{2\text{peak}}$, mL/kg/min, 21.2 ± 5.5 vs. 27.2 ± 6.6, $P = 0.001$), maximum work load (W, 110.4 ± 34.8 vs. 153.0 ± 39.8, $P = 0.0001$), duration of exercise (min, 16.3 ± 2.6 vs. 19.6 ± 2.9, $P = 0.0001$), heart rate reserve (number of beats, 35.4 ± 16.9 vs. 16.6 ± 9.7, $P = 0.0001$), FVC (%), FEV1 (%), FEV1/FVC, VO$_2$, Oxygen consumption, FVC: forced vital capacity, FEV1: forced expiratory volume in the 1st second.

Table 1. Patients’ pretreatment and control group exercise test and SFT parameters.

|                      | AS (n = 28)       | Control (n = 28) | P-value |
|----------------------|------------------|------------------|---------|
| $\text{VO}_{2\text{peak}}$ (mL/kg/min) | 21.2 ± 5.5       | 27.2 ± 6.6       | 0.001   |
| Maximum work capacity (W) | 110.4 ± 34.8     | 153 ± 39.8       | 0.0001  |
| Duration of exercise (min) | 16.3 ± 2.6       | 19.6 ± 2.9       | 0.0001  |
| Heart reserve rate (number of beats) | 35.4 ± 16.9      | 16.6 ± 9.7       | 0.0001  |
| FVC (%)               | 94.2 ± 15.4      | 104.8 ± 14.6     | 0.011   |
| FEV1 (%)              | 98.8 ± 14.9      | 108.8 ± 11.6     | 0.007   |
| FEV1/FVC              | 87.6 ± 4.9       | 88.6 ± 6.2       | 0.719   |

Table 2. Pretreatment and 4th month clinical and laboratory parameters of patients with ankylosing spondylitis.

|                      | Pretreatment (n = 28) | Posttreatment (n = 28) | P-value |
|----------------------|-----------------------|------------------------|---------|
| Chest expansion (cm) | 3.3 ± 1.3             | 4 ± 1.6                | 0.0001  |
| Modified Schober test (cm) | 13 ± 1.7           | 13.8 ± 1.6            | 0.002   |
| BASDAI               | 6.1 ± 1.4             | 2.9 ± 1.4              | 0.0001  |
| BASMI                | 8.2 ± 2               | 6.9 ± 1.8              | 0.0001  |
| BASFI                | 4.7 ± 2.7             | 2.4 ± 2.4              | 0.0001  |
| ASQoL                | 11.8 ± 4.6            | 4.9 ± 4.2              | 0.0001  |
| ESR (mm/s)           | 39.2 ± 23             | 15.5 ± 13.7           | 0.0001  |
| CRP (mg/DL)          | 1.5 ± 1.1             | 0.5 ± 0.7              | 0.0001  |
| $\text{VO}_{2\text{peak}}$ (mL/kg/min) | 21.2 ± 5.5         | 24 ± 5.5               | 0.001   |
| Maximum work capacity (W) | 110.4 ± 34.8       | 132.9 ± 37.2          | 0.0001  |
| Duration of exercise (min) | 16.3 ± 2.6        | 17.6 ± 2.9            | 0.001   |
| Heart rate reserve (number of beats) | 35.4 ± 16.9      | 16.6 ± 9.7            | 0.0001  |
| FVC (%)              | 94.2 ± 15.4          | 95.8 ± 13.8           | 0.478   |
| FEV1 (%)             | 98.8 ± 14.9          | 100.0 ± 14.8          | 0.575   |
| FEV1/FVC             | 87.9 ± 7.0           | 87.6 ± 5.3            | 0.967   |

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, FVC: forced vital capacity, FEV1: forced expiratory volume in the 1st second; $P < 0.05$ was regarded as statistically significant.
and cardiopulmonary capacity, and comparison of these between the two groups, revealed statistically significant differences. These findings objectively show that the work capacity of patients with AS was lower than that of the healthy control group. The aim of treatment in AS is to reduce pain, stiffness, and fatigue; to establish and maintain proper posture; and to ensure physical and psychosocial functionality (11). The entry into use of anti-TNF alpha drugs represented a turning point in the treatment of AS. Studies involving anti-TNF alpha have reported significant improvements in quality of life and acute phase responses in addition to BASDAI, BASFI, and BASMI scores (17–19). However, findings regarding the effects on radiographic progression and extraarticular involvements are inconsistent (20–23). Activity scores in our patients improved significantly in a short time. A significant improvement in patients’ BASDAI (from 6.1 ± 1.4 to 2.9 ± 1.4), BASFI (from 4.7 ± 2.7 to 2.4 ± 2.4), BASMI (from 8.2 ± 2 to 6.9 ± 1.8), ASQoL (from 11.8 ± 4.6 to 4.9 ± 4.2), ESR (from 39.2 ± 23 to 15.5 ± 13.7), and CRP (from 1.5 ± 1.1 to 0.5 ± 0.7) values (P = 0.0001) was achieved with anti-TNF alpha therapy, as well as clinical and laboratory benefits and an improved quality of life. Disease-related loss of work capacity is widespread in AS. Twenty-four percent of employed subjects with AS were identified as receiving help from colleagues, and that assistance was observed more in patients doing physical work and during periods of more active disease findings (24). In a study of 21 patients with AS, Çağar et al. determined that loss of productivity in working life was correlated with onset of disease at advanced age, prolonged delay in diagnosis, and various physical impairments such as spinal mobility and hip involvement (10). Anti-TNF alpha therapies reduce inflammation in AS and contribute to better functionality and work capacity. Studies involving fatigue and functional indices in AS generally measure effectiveness in a subjective manner, although the reliability of data of patient origin is controversial. The ASDAS, a questionnaire containing laboratory markers (ESR and CRP), was therefore developed for that reason and began being used in daily practice (25). Fatigue, loss of work capacity, and effort intolerance are some of the most common symptoms in patients with AS. Our study was planned to show the effect on work capacity and effort tolerance and the effect of anti-TNF alpha therapy on those indices, in an objective manner, in addition to activity indices. There are no previous studies on this subject. In terms of objective evidence, our study demonstrated a statistically significant increase in patients’ aerobic capacity (VO\textsubscript{2peak} mL/kg/min, from 21.2 ± 5.5 to 24 ± 5.5, P = 0.001), maximum tolerable work rate (W, from 110.4 ± 34.8 to 132.9 ± 37.2, P = 0.0001), and duration of exercise (from 16.3 ± 2.6 min to 17.6 ± 2.9 min, P = 0.001) upon assessment at the 4th month of treatment. No previous studies have been performed using this method. To the best of our knowledge, ours is the first study to show, in an objective manner, that anti-TNF alpha therapies increase aerobic capacity. The limitations of the study are relatively low number of patients involved and the short follow-up time. Further studies involving more subjects and longer periods are now needed.

In conclusion, in addition to having positive effects on inflammatory parameters and quality of life in patients with AS, anti-TNF alpha therapy can achieve rapid and significant improvement in parameters objectively demonstrating the patient's cardiopulmonary health status, such as VO\textsubscript{2peak}, maximum work capacity, and duration of exercise. Considering that these patients received treatment for symptoms before anti-TNF alpha, in addition to confirming that the disease leads to a low work capacity, the low work capacity VO\textsubscript{2peak} also shows that standard treatment before anti-TNF alpha was unable to prevent this effect. However, even over a 3-month period, anti-TNF alpha therapy not only controlled disease activity but also (maybe secondary to this) significantly increased cardiopulmonary exercise capacity. These findings may represent an additional and concrete justification for transition to anti-TNF alpha therapy.

References

1. Vernon-Roberts B. Ankylosing spondylitis: pathology. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, editors. Rheumatology. Philadelphia, PA, USA: Mosby; 2003. pp. 1205-10.
2. Miller JM, Sproule BJ. Pulmonary function in ankylosing spondylitis. Am Rev Respir Dis. 1964; 90: 376-382.
3. Landewé R, Dougados M, Mielants H, van der Tempel H, van der Heijde D. Physical function in ankylosing spondylitis is independently determined by both disease activity and radiographic damage of the spine. Ann Rheum Dis 2009; 68: 863-867.
4. Vander Esch M, Van’t Hul AJ, Heijmans M, Dekker J. Respiratory muscle performance as a possible determinant of exercise capacity in patients with ankylosing spondylitis. Aust J Phys 2004; 50: 41-45.
5. Dougados M, Baeten D. Spondyloarthritides. Lancet 2011; 377: 2127-2137.
6. Dagfinrud H, Vollstad NK, Loge JH, Kvien TK, Mengshoel AM. Fatigue in patients with ankylosing spondylitis: a comparison with the general population and associations with clinical and self-reported measures. Arthritis Rheum 2005; 53: 5-11.
ÇAPKIN et al. / Turk J Med Sci

7. van Tubergen A, Coenen J, Landewé R, Spoorenberg A, Chorus A, Boonen A, van der Linden S, van der Heijde D. Assessment of fatigue in patients with ankylosing spondylitis: a psychometric analysis. Arthritis Rheum 2002; 47: 8-16.

8. Turan Y, Duruöz MT, Bal S, Guvenc A, Cerrahoglu L, Gurgan A. Assessment of fatigue in patients with ankylosing spondylitis. Rheumatol Int 2007; 27: 847-852.

9. Bodur H, Ataman S, Rezvani A, Buğdayci DS, Cevik R, Birtane M, Akıncı A, Altay Z, Gürsoy R, Yener M et al. Quality of life and related variables in patients with ankylosing spondylitis. Qual Life Res 2011; 20: 543-549.

10. Capkin E, Taskaynatan MA, Dincer U, Kiralp MZ, Durmus O, Ozgütlü A. Work disability in ankylosing spondylitis: differences among working and work-disabled patients. Clin Rheumatol 2009; 28: 1309-1314.

11. Braun J, van den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, Collantes-Estevez E, Doganirud H, Dijkmans B, Dougados M, Emery P et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011; 70: 896-904.

12. Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. Principles of Exercise Testing and Interpretation. 4th ed. Philadelphia, PA, USA: Lippincott Williams & Wilkins; 2005.

13. Bassett DR, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000; 32: 70-84.

14. Balady G, Arena R, Siesjesma KE, Myers J, Coke L, Fletcher GF. American Heart Association scientific statement: a clinician’s guide to cardiopulmonary exercise testing in adults. Circulation 2010; 122: 191-225.

15. ERS Task Force, Palange P, Ward SA, Carlsen KH, Casaburi R, Gallagher CG, Gosselin R, O’Donnell DE, Puente-Maestu L, Schols AM et al. Recommendations on the use of exercise testing in clinical practice. Eur Respir J 2007; 29: 185-209.

16. Davis J, Van der Heijde D, Dougadas M, Woolley JM. Reductions in health-related quality of life in patients with ankylosing spondylitis and improvements with etanercept therapy. Arthritis Rheum 2005; 53: 494-501.

17. Braun J, Baraliakos X, Listing J, Fritz C, Alten R, Burmester G, Krause A, Schewe S, Schneider M, Sörensen H et al. Persistent clinical efficacy and safety of anti-tumour necrosis factor alpha therapy with infliximab in patients with ankylosing spondylitis over 5 years: evidence for different types of response. Ann Rheum Dis 2008; 67: 340-345.

18. Calin A, Dijkmans BA, Emery P, Hakala M, Kalden J, Leirisalo-Repo M, Mola EM, Salvarani C, Sanmarti R, Sany J. Outcomes of a multicentre randomised clinical trial of etanercept to treat ankylosing spondylitis. Ann Rheum Dis 2004; 63: 1594-1600.

19. van der Heijde D, Kivitz A, Schiff MH, Sieper J, Dijkmans BA, Braun J, Dougados M, Reveille JD, Wong RL, Kupper H et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. ATLAS Study Group. Arthritis Rheum 2006; 54: 2136-2146.

20. Baraliakos X, Listing J, Brandt J, Haibel H, Rudwaleit M, Sieper J, Braun J. Radiographic progression in patients with ankylosing spondylitis after 4 yrs of treatment with the anti-TNF-alpha antibody infliximab. Rheumatology (Oxford) 2007; 46: 1450-1453.

21. van der Heijde D, Salonen D, Weissman BN, Landewé R, Maksymowycz WP, Kupper H, Ballal S, Gibson E, Wong R; ATLAS Study Group. Assessment of radiographic progression in the spines of patients with ankylosing spondylitis treated with adalimumab for up to 2 years. Arthritis Res Ther 2009; 11: 127-145.

22. Baraliakos X, Haibel H, Listing J, Sieper J, Braun J. Continuous long-term anti-TNF therapy does not lead to an increase in the rate of new bone formation over 8 years in patients with ankylosing spondylitis. Ann Rheum Dis 2014; 73: 710-715.

23. Capkin E, Karkucak M, Kiris A, Durmus I, Karaman K, Karaca A, Tosun M, Ayar A. Anti-TNF-α therapy may not improve arterial stiffness in patients with AS: a 24-week follow-up. Rheumatology (Oxford) 2012; 51: 910-914.

24. Ward MM, Kuzis S. Risk factors for work disability in patients with ankylosing spondylitis. J Rheumatol 2001; 28: 315-321.

25. Machado P, Landewé R. Spondyloarthritis: Is it time to replace BASDAI with ASDAS? Nat Rev Rheumatol 2013; 9: 388-392.