

Managing the impact of ankylosing spondylitis on the patient and society

The purpose of this article is to consider the challenges faced by patients and clinicians in relation to long-term management of ankylosing spondylitis, a common rheumatic disease with an early age of onset, and to provide evidence-based recommendations for minimizing the impact of ankylosing spondylitis on the patient and society. The article is organized into three main sections; the first provides a general background in relation to epidemiology, pathogenesis, clinical features, diagnosis and classification; the second considers the impacts of ankylosing spondylitis on the patient and society; the third provides recommendations for minimizing these impacts. In particular, the importance of patient education, group exercise, ergonomic adjustment of the work environment, psychological therapies and spa therapies are highlighted. We also urgently recommend notifying patients of the advantages associated with active membership of a patient support group. Some general conclusions regarding the goals for long-term management of this condition are presented and we consider how the field might develop in the future. Necessary research fields for the future are highlighted.

KEYWORDS: ankylosing spondylitis ■ anxiety ■ depression ■ economic cost ■ fatigue ■ quality of life ■ sexual function ■ sleep ■ work disability

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Ankylosing spondylitis & the spondylarthritides

Ankylosing spondylitis (AS) is the prototype of a group of rheumatic diseases referred to as spondyloarthritides (SpAs). SpAs also include Reiter's syndrome, reactive arthritis, psoriatic arthritis, arthritis associated with inflammatory bowel disease and undifferentiated SpA [1]. Until the 1970s these diseases were considered variants of rheumatoid arthritis (RA), but are now recognized as being distinct from RA, genetically linked (associated with the HLA-B27 antigen) and sharing common clinical and radiologic manifestations [2,3]. The leading clinical symptoms for all SpA subtypes are inflammatory back pain and/or asymmetrical arthritis (predominantly of the lower limbs), enthesitis (inflammation of the tendinous or ligamentous attachment to the bone) and anterior uveitis (inflammation of the middle layer of the eye) [2,4].

■ Epidemiology & pathogenesis

Ankylosing spondylitis is one of the most common rheumatic diseases, affecting between 0.5 and 14 per 100,000 people per year [2,3]. The prevalence is between 0.1 and 1.4%, with most data coming from Europe [2]. Symptoms usually appear in the second or third decade and men are two- to three-times more likely to be

diagnosed with AS than women [5]. The cause of AS is unknown, although both genetic and environmental factors are likely to be implicated [2]. Around a third of the genetic effect is explained by HLA-B27 and rates vary between countries in relation to the prevalence of this antigen in the population [3,6]. Genes outside the HLA region are also believed to be involved but are yet to be identified [2].

■ Clinical features

The term 'ankylosing spondylitis' literally means inflammation and fusing of the vertebrae (from the Greek, ankylosing – 'fusing together' – and spondylitis – 'inflammation of the vertebrae'), although the disorder is now recognized as a systemic disease [7]. Apart from often affecting the complete axial skeleton, AS may involve peripheral joints (most commonly the hips, shoulders and ribcage joints) and cause numerous extraskeletal manifestations [7,8]. Acute anterior uveitis occurs in up to 40% of patients, psoriasis in 9% and overt clinical inflammatory bowel disease in 5–10% [7,8]. Subclinical intestinal inflammation is also common in AS patients and around 6.5% of these patients will later develop overt Crohn's disease [8].

The disease course varies widely between patients and is difficult to predict for any given individual; while some have minimal

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involvement, in others progressive widespread disease results in poorer functional outcomes and even death [5]. Men tend to have more severe involvement in the spine, while more frequent involvement of peripheral joints is seen in women [9], and early (juvenile) onset AS is associated with higher prevalence of hip involvement [10]. HLA-B27 positivity is associated with earlier age of onset, higher disease activity, poorer functional status and more extra-articular manifestations [11]. Retrospective studies suggest that hip involvement is a bad prognostic sign and that structural damage at presentation is the best predictor of further damage [2].

The Assessment in SpondyloArthritis international Society (ASAS) [101] and European League Against Rheumatism (EULAR) [102] recommend that disease monitoring of patients with AS should include patient history, clinical parameters, laboratory tests and imaging, as well as the ASAS core set [12]. The core set includes recommended instruments for assessment of axial, peripheral and enthesopathological manifestations (TABLE 1).

■ Diagnosis & classification

Diagnosis of AS is challenging, particularly in the early stages, since chronic back pain and manifestations of peripheral disease have to be differentiated from other causes, including other rheumatic diseases and mechanical pain syndromes [4]. Evidence of radiologic changes is necessary for definitive diagnosis [13], although such changes are often slow to develop and may remain normal for several years after the onset

of pain, stiffness and inflammation [4,14]. It is common for patients to experience symptoms for up to 10 years before diagnosis [15].

Recently, efforts have been made to develop criteria that allow earlier diagnosis and classification of patients with AS, using MRI technology to detect inflammation at an early stage. ASAS has published a set of criteria for 'axial SpA' (early AS and undifferentiated axial SpA as its possible preform), which allow for detection of sacroiliitis by x-ray or MRI [16]. If this evidence is combined with one or more SpA feature in patients with chronic inflammatory back pain, the patient can be classified as axial SpA. Patients who are HLA-B27 positive and fulfill two further SpA features can also be classified as axial SpA. Inflammatory back pain is present if four out of five of the following parameters are present [16]:

- Age at onset of less than 40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night (with improvement on getting up)

The ASAS classification criteria for axial SpA are shown in FIGURE 1. ASAS suggests that these criteria will perform well as diagnostic criteria if applied in a rheumatology setting with a high pretest probability of axial SpA in patients referred due to inflammatory back pain, although it remains to be seen how they will perform in settings with a lower prevalence of SpA [17].

Table 1. Assessment of SpondyloArthritis international Society core sets.

Domain	Core set			Instruments
	CR	SMARD/PT	DC-ART	
Physical function	x	x	x	BASFI or Dougados Functional Index
Pain	x	x	x	VAS in the past week, spine at night, due to AS and VAS in the past week, spine due to AS
Spinal mobility	x	x	x	Chest expansion and modified Schober and occiput to wall distance (BASMI or lateral side flexion)
Patient's global assessment	x	x	x	VAS in the past week
Stiffness	x	x	x	Morning stiffness
Peripheral joints and entheses	x		x	Number of swollen joints and assessment of painful entheses
Acute phase reactants	x		x	ESR
Fatigue			x	VAS question on fatigue from BASDAI
Imaging			x	AP and lateral x-ray examination of the lumbar spine, lateral cervical spine and AP pelvis (SI and hip joints)

AP: Anteroposterior; AS: Ankylosing spondylitis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CR: Clinical record keeping; DC-ART: Disease-controlling antirheumatic treatment; ESR: Erythrocyte sedimentation rate; PT: Physical therapy; SI: Sacroiliac; SMARD: Symptom-modifying antirheumatic drug; VAS: Visual analogue scale.
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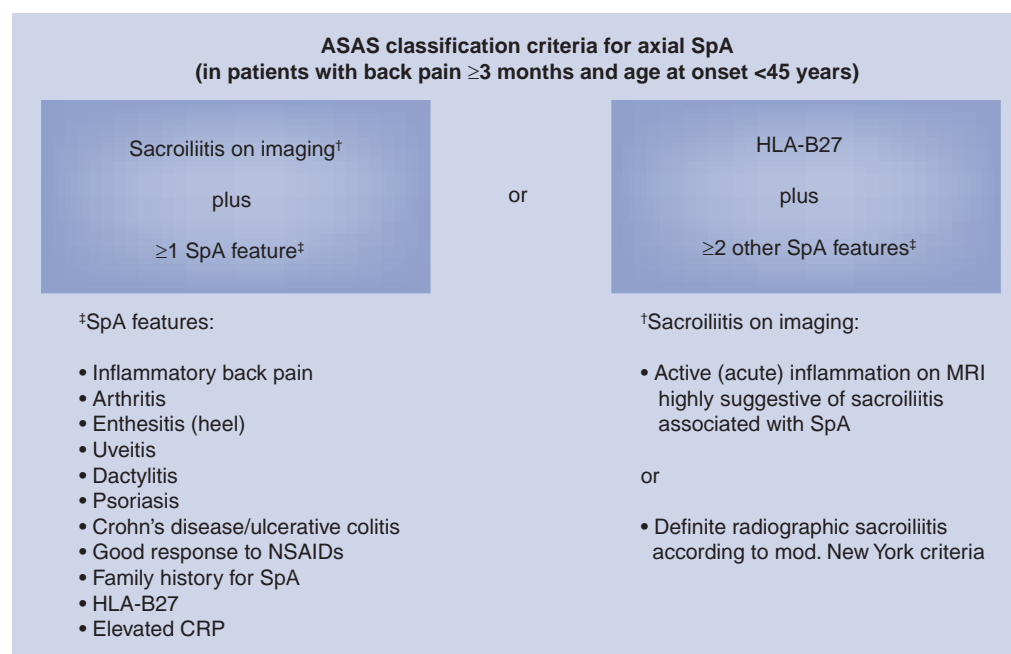


Figure 1. Final set of classification criteria for axial spondyloarthritis selected by the Assessment of SpondyloArthritis international Society. Sensitivity: 82.9%, specificity 84.4%; n = 649 patients with chronic back pain and age at onset < 45 years. Imaging arm (sacroiliitis) alone has a sensitivity of 66.2% and a specificity of 97.3%.

*Note: elevated CRP is considered a SpA feature in the context of chronic back pain.

ASAS: Assessment of SpondyloArthritis international Society; CRP: C-reactive protein; Mod.: Moderate; NSAID: Nonsteroidal anti-inflammatory drug; SpA: Spondyloarthritis.

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Impacts of AS on the patient & society

■ Implications for quality of life & social functioning

A number of studies have revealed significantly lower quality of life in AS patients compared with healthy populations, particularly in relation to physical functioning [18–20]. Impacts of AS on the patient include pain, stiffness, fatigue, sleep problems, treatment side effects, concerns about appearance, worry about the future, and interference with leisure activities and activities of daily living [20,21]. Patients may also experience changes in mood and difficulties with family and social relationships [21,22], and many find it difficult to remain in employment. Several studies have revealed high rates of unemployment, early retirement and lost work days among AS patients [23–25]. Work disability is associated with lower quality of life in patients with AS and has been linked to demographic factors (higher age, lower education level), disease characteristics (higher disease activity, poorer physical function, pain, spinal fusion, uveitis, hip replacement), job characteristics (having a more physically demanding job) and psychosocial factors (a passive coping style and insufficient support from colleagues/managers) [23,26–28].

Problems with sexual functioning have also been reported, although findings are not consistent across studies. For example, lower scores have been reported for AS patients compared with healthy controls for sexual drive, erection, problem assessment and overall satisfaction according to the Brief Males Sexual Function Inventory (BMSFI) [29], although a study of sexual motivation in AS patients revealed no significant difference between patients and healthy controls [30]. One study revealed lower erectile function, orgasmic function, intercourse satisfaction and overall satisfaction scores according to the International Index of Erectile Function (IIEF) in men with AS compared with healthy controls [31], while another found no significant difference between IIEF domain scores of AS patients and healthy controls, except for the sexual desire domain [32]. These inconsistent findings may be due to differences in sample characteristics. For example, sexual problems in AS patients have been linked to disease characteristics (duration of morning stiffness, limited joint mobility), and to depression and anxiety [29,31–33].

■ Individual & demographic differences

A number of studies have highlighted demographic differences in quality of life and

psychosocial wellbeing among AS patients. For example, Barlow *et al.* report that approximately a third of patients with AS experience a high level of depressive symptoms and women report more depression than men [34]. In this study, pain was a major determinant of depression for women, but was of lesser importance for men. Ward found that women were two- to three-times more likely than men to report concerns with fatigue, coping with illness, job performance and self-care tasks; women experienced more pain than men and more role limitations due to physical problems [20]. Low level of education has also been linked to poorer quality of life in AS patients [19,20,24,26].

Individual differences exist in patients' perceptions of the impacts of AS. For example, implications of AS for employment are not necessarily perceived as negative. Barlow *et al.* interviewed six patients regarding their experiences of working with AS [26]. For some, work changes associated with AS were perceived as negative, resulting in frustration, low self-esteem and lack of self-confidence. However, others reported that they felt less pressure to compete in the work place and found enjoyment in new activities and roles. Hamilton-West and Quine also found that changes associated with AS can be perceived as both negative and positive [21]. In this study patients cited a number of positive impacts of AS, including healthier lifestyle, social benefits (e.g., making new friends via support groups, spending more time with loved ones), a feeling of strength and determination, increased empathy for the suffering of others, and a more positive perspective on life. Such findings indicate that the implications of AS for the patient are complex and it is important to not only assess what has changed in the patient's life as a result of their condition, but also how these changes are perceived by the patient.

■ Economic costs of AS

Implications of AS for employment can also be considered from an economic perspective. A number of studies have assessed the cost of AS, both for the patient (e.g., income loss, out-of-pocket costs) and society (including direct medical and nonmedical care costs, and lost productivity). Costs of illness to society can be calculated using the friction costs method or the human capital (HC) approach. The former limits the period of sick leave until the worker has been replaced, while the latter includes productivity costs from the first until the last day of absence from work (i.e., until return to work or retirement, whichever

comes first) [24,25,35]. Boonen *et al.* calculated costs for patients living in The Netherlands, France and Belgium [24,25,36]. The mean total annual costs to the patient (healthcare costs, nonhealthcare costs and income loss combined) were €1795 per person, with income loss accounting for 76% of the total patient costs. Nonhealthcare costs incurred by AS patients included expenditure for private household help, transportation costs and contributions to societies or exercise groups. The cost to society due to lost productivity varied widely between the three countries. In The Netherlands, the annual cost per patient was €1257 using the friction costs method and €8862 using the HC method. In France and Belgium, annual costs were €428 and 476, respectively, using the friction costs method; costs calculated using the HC method were also similar in France (€3188) and Belgium (€3609). Ward calculated total annual costs (direct and indirect costs) of AS in the USA using the HC method [37]. Annual total costs averaged US\$6720 per patient, with indirect costs (lost productivity) accounting for 74% of the total cost. Direct costs (costs of medical and nonmedical care) per patient were \$1775.

Differences in methodology between the US and European studies make it difficult to compare directly between countries, although it is evident that AS has significant cost implications for the patient and that loss of productivity is the major driver of societal costs. However, because of the low prevalence of the disease, the costs related to AS are a relatively small part of the costs of all diseases to society [35]. Studies comparing costs of AS to other chronic conditions have reported lower costs of AS compared with RA, fibromyalgia and chronic low back pain [38–40].

Recommendations for minimizing the impacts of AS

Since AS has the capacity to impact both physical and psychosocial functioning, long-term management is likely to necessitate a combination of drug treatments, physical therapies and psychosocial interventions [21,41,42]. ASAS and EULAR have published joint recommendations for management of AS, based on best available evidence [12]. This should be read in conjunction with national guidelines, such as the NICE in the UK [103]. In relation to treatment of AS, the ASAS/EULAR review concluded that:

- Optimal management of AS requires a combination of pharmacological and nonpharmacological treatments; these are complementary and both are of value in the initial and

continuing treatment of patients with AS. Nonpharmacologic treatments supported by clinical trial evidence include exercise, patient education and behavioral therapy;

- Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors are equally effective in improving pain and function. Choice of nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors should be based on the patient's gastrointestinal risk profile and take account of concomitant risk factors for cardiovascular disease;
- Anti-TNF treatment should be given to patients with persistently high disease activity despite conventional treatments; although significantly more expensive than traditional AS treatments, improvements in pain and function may outweigh the costs in a formal cost-benefit analysis. Further economic evaluation is needed to confirm this;
- There is little evidence for the efficacy of disease-modifying antirheumatic drugs, such as sulfasalazine and methotrexate, although sulfasalazine may be considered for patients with peripheral joint symptoms. There is no evidence to support the obligatory use of disease-modifying antirheumatic drugs before, or concomitant with, anti-TNF treatment in patients with axial disease;
- Use of systemic corticosteroids for axial disease is not supported by evidence, although corticosteroid injections directed to the site of musculoskeletal inflammation may be considered.

This article only includes studies with clinical outcomes for AS (disease activity, physical function and structural damage). In the context of the present article, it is important to also consider how best to address the psychosocial and socio-economic impacts of AS. In the following sections we will consider the efficacy of pharmacological and nonpharmacological interventions for reducing the impacts of AS on quality of life (fatigue, sleep problems, self-image, mood, relationships and sexual functioning) and work disability (an important determinant of quality of life and the main driver of societal costs).

■ Fatigue & sleep problems

Fatigue is a common problem in AS, affecting around 65% of patients [43,44], and quality of life is significantly reduced in these patients [45]. Measurement of fatigue is incorporated into the Bath Ankylosing Spondylitis Disease Activity

Index (BASDAI) [46]. However, fatigue is not only related to disease activity, but also to a host of other factors including associated diseases, side effects of drugs, depression and sleep disorders [45]. Therefore, it is important to identify factors contributing to fatigue in AS patients and to offer appropriate treatment.

Available evidence suggests that anti-TNF therapy may ameliorate fatigue more than nonsteroidal anti-inflammatory drugs, and that regular physical activity and spa therapy may help to reduce fatigue [45]. Obstructive sleep apnoea can also occur in patients with AS and detection and treatment of sleep apnoea syndrome can improve fatigue symptoms in these patients [47]. Recent research indicates a particularly high prevalence of obstructive sleep apnoea syndrome in patients aged over 35 and in those with disease duration of 5 years or longer [48]. Fatigue may also be reduced by treating depression or improving sleep either pharmacologically or via lifestyle modifications/cognitive behavioral therapy (CBT) [49]. Abad *et al.* suggest an algorithm for rheumatic diseases with associated sleep disorders [49]. This is summarized below:

- Review medications for sleep side effects and discontinue/reduce the dose/prescribe an alternative;
- Look for an associated primary sleep disorder (e.g., sleep apnoea) and treat the underlying disorder;
- Evaluate for insomnia (sleep onset, sleep maintenance, early awakening or poor quality sleep). Examine environment/lifestyle factors and consider CBT or pharmacotherapy;
- Screen for depression and anxiety. Consider CBT, pharmacological therapy or stress management;
- Refer to social services and support groups for disability/psychosocial issues contributing to the mood disorder;
- Address pain issues that can affect sleep; refer to physical/occupational therapy for ancillary treatment and consider adjunctive pain therapies (e.g., transcutaneous electrical nerve stimulation);
- Use available pharmacological interventions for pain, depression, anxiety and insomnia;
- Set short- and long-term goals and action plans with the patient. Encourage general conditioning and regular exercise to maintain activities of daily living; patients who have difficulty mobilizing against gravity may benefit from exercises in a warm pool.

■ Mood, self-image & relationships

Regular exercise is not only important for maintaining activities of daily living, but can also help to relieve stress and maintain psychological wellbeing. Exercising as a member of a group can also help to build positive relationships with other patients [21]. A recent Cochrane review of physiotherapy for AS patients concluded that both home-based and supervised exercise programs improve movement and physical function, but patient global assessments (BAS-G scores) were significantly better among patients attending supervised group physiotherapy [50]. Patient global assessments were further improved by adding 3 weeks of exercise at a spa resort (e.g., the Radon Spa resort in Bad Hofgastein, Austria [51]).

However, research also indicates that, although AS patients are aware of the benefits of exercise, the majority do not exercise on a regular basis [52]. This problem is not specific to AS patients – adherence to long-term treatment regimes involving a behavioral component is consistently lower than adherence to medication, and exercise programs are associated with high rates of attrition [53]. Patient support groups play an important role in maintaining regular exercise. AS patients who attend support groups tend to comply more with exercise treatment and be less reliant on medical personnel to control their health [34,54]. By contrast, patient education without ongoing support does not result in sustained improvement in exercise behavior, although it is effective in improving depression and self-efficacy [53].

It is important to note that not all patients have the opportunity (or desire) to attend a support group and it is necessary to consider other methods of providing psychosocial support for these patients. For example, Hamilton-West and Quine [55] reported beneficial effects of expressing emotions via a structured writing task and several studies have reported positive impacts of similar tasks in rheumatoid arthritis patients [56–58]. Patients who do not wish to attend support groups can also be provided with details of patient helplines and websites for information and advice. It is unlikely, however, that these forms of support will provide all of the advantages associated with active membership of a patient support group. Therefore, it is important that AS patients are aware of the existence of support groups and the range of support available to members [59].

Optimal disease management is of vital importance for minimizing the impact of AS on mood and personal relationships. Anti-TNF therapy has the capacity to significantly improve

quality of life for AS patients across all domains, including emotional wellbeing and emotional and social role functioning [18].

■ Sexual functioning

In order to minimize the impact of AS on sexual functioning, it is important that patients are able to present problems and concerns without embarrassment [60]. Health professionals should encourage open communication regarding sexual problems and offer treatment appropriate to the patient's specific symptoms (e.g., sildenafil for erectile dysfunction) as well as general recommendations including: discussion of problems with the partner (e.g., regarding partner's fear of causing pain or distress during intercourse), using analgesics, heat or muscle relaxants before sexual activity to reduce pain, exploring different positions or alternative methods of sexual expression [60,61].

Sexual function and family planning should also be discussed when planning or reviewing treatments, since some drugs used in the treatment of rheumatic diseases can interfere with fertility, either because of their harmful effects on pregnancy and the fetus, or because of gonadotoxicity [62]. Anti-TNF therapy can improve erectile function, intercourse satisfaction and sexual desire in male AS patients [63], and may reduce infertility in women with AS [64], although women wishing to conceive must be advised against use of anti-TNF therapy during pregnancy until extensive reports have clearly demonstrated their safety for the mother and fetus [64].

Open discussion with AS patients regarding sexual relationships might also highlight further support needs. For example, relationship problems in patients with AS may arise due to mood disturbance (e.g., feeling irritable) or concerns regarding appearance/body image. Patients may also worry about 'becoming a burden to their partner' [21]. Patients raising such concerns may be referred for relationship counseling or psychological therapies (e.g., CBT). Support groups may also provide valuable advice and support for these patients.

■ Work disability

As discussed previously, the cause of work disability in patients with AS is multifactorial and includes demographic factors, disease characteristics, job characteristics and psychosocial factors. Chorus *et al.* examined the relative importance of these factors in predicting withdrawal from the labor force and found that a passive style of coping, characterized by pacing to cope with limitations, was the most relevant factor [27]. Technical and ergonomic adjustment of the workplace was also

important for reducing the risk of withdrawal. Simple changes to the work environment such as flexible working hours, ability to move around frequently and the purchase of ergonomically designed office furniture may help to alleviate fatigue or physical discomfort in AS patients and reduce the risk of withdrawal from the labor force [26]. Patients should also be warned against working in cramped, flexed positions, standing for long periods of time or working in cold conditions, since these factors may increase pain and risk of long-term work disability [27].

Patients with AS may benefit from advice and guidance relating to health and safety at work. For example, in the UK the Health and Safety Executive provides guidance in relation to management and prevention of back pain at work [104], and the National Ankylosing Spondylitis Society provides advice regarding posture at work and practical adaptations to overcome difficulties such as driving with back and neck problems [105]. National AS societies currently exist in 30 countries – for further information and contact details see the Ankylosing Spondylitis International Federation website [106].

Conclusion

Ankylosing spondylitis is a common rheumatic disease that affects people at an early stage in their working lives and at a point when many will be forming long-term relationships or planning a family. There is no cure for this disease and the goal for long-term management is to keep pain and inflammation under control, while maintaining spinal mobility and physical function, and minimizing impact on quality of life. Minimizing work disability associated with AS is important, both for maintaining quality of life and for reducing the economic costs of the disease. While costs to the individual patient can be significant, the costs to society are relatively low compared with other chronic conditions.

Choice of pharmacological therapies for patients with AS should follow existing guidance, although it is also important to consider potential impacts of medications on sleep and sexual functioning, and to discuss issues surrounding family planning. For some patients, additional treatments may be necessary to address problems such as sleep apnoea and erectile dysfunction. Nonpharmacological treatments (exercise, patient education and psychological therapies) are an important part of long-term management and can help to minimize the impact of AS on quality of life. Exercise is likely to be most beneficial when conducted in a group with other patients.

Regular physical exercise combined with spa therapy may help to reduce fatigue and maintain psychological wellbeing, as well as maintaining activities of daily living. Adjunctive pain therapies (e.g., transcutaneous electrical nerve stimulation or heat) may help to improve sleep and reduce pain associated with sexual activity – patients should be encouraged to discuss difficulties in relation to fatigue and relationship/sexual problems in order that appropriate treatment and support may be offered.

It is important that AS patients are able to access advice regarding health and safety at work, since relatively simple technical and ergonomic adjustment of the work environment could help to prevent or delay withdrawal from the labor force. Patient support organizations provide a wide range of advice and support to people with AS and all patients should be provided with contact details for local/national support groups.

Future perspective

Several recent developments in the field have potentially important implications for managing the impact of AS on the patient and society. It will be important to continue to monitor and evaluate the impacts of these developments in the coming years. The development of criteria for early diagnosis and classification is likely to have significant implications for reducing the long delay many patients experience between onset of symptoms and diagnosis. It will be important to determine how these criteria perform in rheumatology settings as well as in settings with low pre-test probability of AS. In 5–10 years it should be possible to determine whether these criteria have resulted in a significant improvement in rates of early diagnosis.

Anti-TNF therapy represents a significant breakthrough in the management of AS, since these treatments have the capacity to improve pain and function in patients who do not experience improvement with conventional treatments. Anti-TNF treatments may also help to improve fatigue, sexual function and fertility, and reduce the impact of the disease on quality of life. However, it will be important to determine their safety for controlling disease activity during pregnancy. Greater knowledge of the risks and benefits of treatments during pregnancy will be beneficial, both for managing active disease in pregnant women with AS and for counseling patients who are considering a future pregnancy [65]. Further research is also needed to evaluate the response of specific features of spondyloarthritis to the different anti-TNF agents – for example, which drug should be

chosen for a patient with uveitis, inflammatory bowel disease or extreme fatigue [66]. It will also be important to determine their benefits for patients with preradiologic axial SpA [67].

The development and evaluation of nonpharmacological treatment approaches for patients with AS is also significant, since optimal management requires a combination of drug treatments, physical therapies and psychosocial interventions. However, further research will be necessary to determine how best to design and deliver nonpharmacological treatments. For example, the recent Cochrane review of physiotherapy for AS patients concluded that interventions are often poorly described and use different types of exercises/training doses without defining the expected physiological responses to exercise programs. Consequently, the optimal exercise program for AS patients could not be determined [50]. Future research should determine what type of intervention to offer to whom (considering demographic differences and disease characteristics) at what point in the disease course. When developing and evaluating interventions, it will also be important to consider practical issues. For example, some studies included in the Cochrane review evaluated effects of exercise at a spa resort in the Dead Sea area, which may not be accessible to all patients with AS. It is also recognized that many patients do not exercise regularly even when they are aware of the benefits of doing so. Interventions

should be designed, not only to improve clinical outcomes, but also to maximize rates of uptake and maintenance.

Research evaluating the impact of AS on quality of life is valuable, since this research highlights important targets for intervention. However, there is no 'gold standard' for measuring quality of life in AS patients and previous research has used a wide range of measures including generic quality of life questionnaires, arthritis-specific measures and AS-specific measures [68]. Future research should determine how best to measure, quality of life in AS patients to ensure that evaluation of the impact on quality of life may be routinely included in trials of new and existing treatments. As discussed earlier, quality of life assessment in AS should include both an evaluation of what has changed in the person's life as a result of their condition and how these changes are perceived by the patient.

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Executive summary

- Ankylosing spondylitis is one of the most common rheumatic diseases, but can be difficult to differentiate from other rheumatic diseases and mechanical pain syndromes, particularly in the early stages.
- In addition to pain, inflammation and fusing of the vertebrae, patients may experience involvement in peripheral joints and numerous extraskelatal manifestations. Symptoms are highly variable and the disease course is difficult to predict.
- Recent developments in diagnosis and classification criteria have the potential to reduce the considerable delay many patients experience between symptom onset and diagnosis; this is particularly important now that more effective treatments are available.

Impacts on the patient & society

- Ankylosing spondylitis occurs at a particularly important stage of life in terms of implications for employment, as well as implications for family and personal relationships. The impact on quality of life varies in relation to demographic factors (e.g., gender, employment status and level of education). Women are at greater risk of depression.
- Ankylosing spondylitis also has financial implications for the patient in terms of healthcare costs, nonhealthcare costs and income loss. Work disability is the main driver of the costs to society, although costs to society are relatively low compared with other chronic conditions.
- Fatigue is a common problem and may be related to a wide range of factors including disease activity, associated diseases, side effects of drugs and sleep disorders. Fatigue has important implications for quality of life.

Recommendations for minimizing the impact of ankylosing spondylitis

- Treatment should follow existing guidance, although it is also important to consider the potential impacts of medications on sleep and sexual functioning, and to discuss issues surrounding family planning.
- It is important to identify the factors contributing to fatigue and/or sexual dysfunction, and offer appropriate treatment in order to minimize impact on quality of life. This may involve changes to medications, physical/psychological therapies and/or treatment of associated disorders. Work disability may be reduced via technological or ergonomic adjustment of the work place.
- Patients should be encouraged to exercise regularly, preferably as a member of a group, and be provided with contact details for local/national ankylosing spondylitis support groups. Patients with depression, relationship difficulties or concerns regarding appearance and self-image may be referred for counseling or psychological therapies (e.g., cognitive behavioral therapy).

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