Optimizing outcomes for ankylosing spondylitis and axial spondyloarthritis patients: a holistic approach to care

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Abstract
Axial SpA (axSpA) can affect diverse elements of an individual’s life. The areas affected can be much more wide-ranging than the historical medical model of SpA, causing increased disease activity (pain and stiffness) and disability (reduced range of movement and physical function). A more holistic view of the individual results in the realization that many other areas of life can be adversely affected by axSpA, from the ability to work effectively and function socially, to effects on quality of life and the onset of worsening fatigue or mood disturbance. A good understanding of these areas outside the medical model allows for an improved understanding of the overall life impact of axSpA. This highlights the importance of understanding how to measure these elements of life using patient-reported outcome measures that can truly reflect an individual’s experience of axSpA. These measures can then provide a better insight into the risks and benefits of interventions and medications used to treat axSpA.

Key words: ankylosing spondylitis, biologic therapy, health-related quality of life, holistic approach, spondyloarthritis, productivity, psychological distress

Rheumatology key messages
• The impact of axial SpA is much wider than physical function, pain and disease activity.
• Axial SpA may affect work, mood, fatigue and quality of life.
• Interventions considered for axial SpA should include a spectrum from psychological counselling to biological.

Introduction
Important advances in the diagnosis and classification of SpA over the past 10 years particularly include the demonstration of spinal inflammation using MRI in the absence of radiographic evidence of change [1, 2]. The diagnosis of axial SpA (axSpA) reflects patients within a spectrum of disease presentations and investigations and ranges from those with radiographic sacroiliac changes (previously referred to as AS) to those with only clinical features suggesting axial inflammation. Patients with axSpA without radiographic evidence of sacroiliitis can now be classified as having non-radiographic axSpA, which does not appear to differ significantly from radiographic axSpA (synonymous with AS) in terms of the main clinical manifestations, disease activity, pain and effect of biologics [3–5]. Although non-radiographic axSpA has less inflammation (lower CRP levels and less spinal inflammation on MRI) and less impairment in spinal mobility compared with AS, the two ends of the spectrum are associated with a similar burden in terms of physical function, mood disturbance, work impact and quality of life impairment [6].

Before the introduction of the Assessment of SpondyloArthritis international Society (ASAS) criteria, the adult prevalence of AS was estimated to be between 0.1 and 1.4%. It varies with geographical region (reflecting varying prevalence of HLA-B27), with the highest rates found in northern Europeans and indigenous North Americans [7–9]. European estimates include a prevalence of 0.9% in Germany [8] and 1.1–1.4% in northern Norway [9], which are markedly higher than estimates in non-Caucasian populations such as Turkey at 0.25% [10] or China at 0.11% [11].

The more inclusive classification criteria will have a considerable impact on the increasing prevalence of SpA, because many patients with previously unclassifiable axSpA can now be identified as having SpA [1]. This has
socioeconomic implications for the overall burden of disease. AxSpA occurs in young adults at the peak of their productive lifespan [2] and is associated with a considerable burden in terms of restrictions in activities of daily living [12, 13] and reduction in health-related quality of life (HRQoL) [13], work productivity and rates of employment [7, 14, 15]. Because axSpA usually starts before 45 years of age, the effect of the disease on different aspects of life (career, family and social life) is of considerable duration.

**Importance of reduction in work productivity on individuals and society**

Reduction in work productivity is an important component of the indirect costs of SpA, which are typically calculated in terms of absenteeism and presenteeism using the Work Productivity and Activity Impairment Questionnaire in AS [16]. Absenteeism is defined as the quantity of potentially disease-related sick leave, whereas presenteeism is defined as patient-reported reduced productivity at work [16].

In a UK study of 612 AS patients [15], employment rates were 14% lower than the UK national average, with 39.5% of patients of working age being unemployed, 44% of whom related this to poor health. In a more recent Italian study [17], axSpA employment rates were slightly lower than in the general population (53% vs 58%), 14% of patients reported axSpA-related discrimination at work and the proportion of patients receiving disability benefits was nearly five times higher than that in the general population (34% vs 7.3%). However, extrapolation of data between AS and axSpA and from one country to another is challenging because of local influencing factors such as local unemployment/disability benefit systems [18].

A number of factors have been found to be associated with work disability and loss of productivity at work. Unemployment is associated with older age, social deprivation, longer disease duration, functional impairment and depression. Absenteeism is associated with worse disease activity and depression, while presenteeism is associated with a wider range of factors including older age, worse disease activity, poorer physical function, lower quality of life, anxiety, depression [15] and a sense of helplessness [19]. Correlations between increased signs and symptoms of disease and reduced productivity suggest that treatments aimed at improving helplessness, reducing anxiety/depression and controlling disease activity could also reduce work disability and loss of productivity [15, 19, 20].

**Frequency of psychological symptoms in axSpA and their impact on patients’ overall well-being**

Psychological distress, including symptoms of depression and anxiety, is an important factor to consider when determining outcomes and quality of life in patients with axSpA. Some studies have described the close association between mood and measures of self-reported disease activity, functional status, educational achievement, deprivation, pain and HRQoL in AS [21–28].

Psychological distress is frequently reported in patients with a variety of rheumatic disorders, more commonly than in the general population [29]. The reported prevalence of depression and anxiety in axSpA is extremely wide, varying between 9 and 56%, and 19 and 60%, respectively [21–28, 30]. Anxiety and depression scores were reported in one study to be similar in AS and in non-radiographic axSpA [24].

Although historically underevaluated because of low numbers of women in studies, recent publications have indicated that women with AS have more depression [21] and anxiety [22] than men with the condition. As in the general population, social deprivation may affect the psychological state of individuals with axSpA [23].

Disease activity scores (including BASDAI and ASDAS-CRP) significantly correlate with both anxiety and depression in AS [24–26, 28], with one study also reporting ESR, a laboratory measure of inflammation, as an independent risk factor for higher anxiety scores [26]. In the one axSpA study to date to examine the relationship between psychological distress and disease activity, only depression (not anxiety) appears to be related to disease activity [24].

Decreased physical function and AS-related restricted range of movement also appear to detrimentally influence mood [24–26]. Both poor disease activity and physical function are also associated with wider psychological characteristics such as passive coping strategies and a sense of helplessness [27, 28].

**Fatigue**

Health economic burden, a major component of which is fatigue, increases steeply with increasing disease activity [31]. Estimates suggest that up to 66% of patients with AS are affected by fatigue [32], comparable to the rate in other long-term inflammatory conditions such as RA [33]. The complex, multi-dimensional nature of fatigue associated with a range of rheumatological conditions has been distinguished from normal everyday tiredness by frequency, persistence, unpredictability and failure to be resolved by rest [34, 35]. Growing acknowledgment of the relative importance of AS fatigue [36] has fuelled interest in its treatment and management [37, 38], and highlighted the need for accurate and credible assessment [38].

Current international guidance for AS fatigue assessment is limited to a single item, the global assessment of severity (BASDAI question 1) [39]. The complex nature of fatigue experienced in AS means that limited assessment potentially fails to identify patients at risk of fatigue-related impairment.

The fatigue related to the inflammatory elements of axSpA may be detrimentally affected by the fatigue from concurrent pain syndromes such as FM [40], which is more common in patients with AS than in the general population. In comparison with a population prevalence of 2–4% [41], a Brazilian study [42] reported a prevalence of FM of 15.0% in patients with AS. This is consistent with
the observation of the high prevalence of FM in inflammatory rheumatic diseases in general [41]. The presence of FM alongside axSpA may influence patients’ perceptions of pain, function and disease activity, and may distort responses to key patient-reported outcome measures such as BASDAI and the BASFI.

**HRQoL**

HRQoL is a broad, multi-dimensional concept that usually includes subjective evaluations of both positive and negative aspects of life. It may be defined as the ‘net consequence of a disease and its treatment on a patient’s perception of his or her ability to live a useful and fulfilling life’ [43]. It is challenging to measure because quality of life has a different meaning for nearly every individual and every disease state. Although health is one of the important domains of overall quality of life, there are other equally important aspects of life that can be affected by illness, such as family life, social support, body image, ability to work, housing, spirituality and socioeconomic status [43].

Despite these challenges, HRQoL questions have become an important component of public health surveillance and are generally considered valid indicators of unmet needs and intervention outcomes. The efficient and cost-effective management of any disease requires competing treatment regimens to be evaluated for their ability to both control disease activity and improve the quality of life of patients.

AS often has a significant impact upon an individual’s HRQoL [44]; the magnitude of this is at least equivalent to that seen in patients with other chronic conditions such as diabetes, arthritis and hypertension [45]. Traditional methods of evaluation—with their focus on the locomotor system, measures of impairment and disease activity—will inevitably fail to describe the extensive multi-dimensional issues associated with axSpA disease.

Given the typical age at onset of the disease and the subsequent progression towards disability with, historically, few therapeutic alternatives, it is perhaps not surprising that patients with axSpA have had such diminished HRQoL. As spinal mobility is progressively lost, or pain levels escalate, difficulty in performing simple physical routines places a huge burden on these patients that extends beyond the physical hardship and compromises the patient’s social and psychological function. Reductions in HRQoL are most pronounced in the more physical and disease activity domains, but are also clearly evident in the psychosocial domains: axSpA leads to changes in mood or personality, low self-esteem, stigma of disease and worry about the future, and adversely affects social life and relationships with friends and family [46]. For example, uncontrolled axSpA disease may threaten the ability of a young adult to remain in employment and hence support their family both financially and emotionally [47]. It may affect them physically, for instance by limiting the amount of sport they can participate in and directly influencing self-perceptions of success in achieving a traditional gender role. Consequently, their ability to fulfil their role as a partner, a parent and a member of society is challenged.

**Overall health and functioning**

Recently, ASAS introduced the first AS-specific health index (ASAS HI), which can be used to measure overall functioning and health [48]. The index contains 17 patient-rated items covering the whole range of International Classification of Functioning, Disability and Health categories, including pain, emotional functions, sleep, sexual functions, mobility, self-care and community life. Patients are asked to respond ‘agree’ or ‘do not agree’ with a statement in each category, resulting in a score from 0 to 17. Unlike the symptom-specific instruments described above, ASAS HI captures whether problems are present in different categories of functioning rather than the subjective experience of those problems [48].

**Therapy for AS**

There is good evidence that treatment with many of the licensed biologic therapies is associated with significant improvements in all aspects of HRQoL, from disease activity, pain and physical functioning to work stability, patients’ psychological health and global quality of life [49–54]. These important changes in the clinical management of axSpA have resulted in the widespread use of biologic therapies.

People with aggressive disease are offered such treatments more commonly, and at an earlier stage in the disease course [55]. The evidence is clear that short-term benefits can be considerable. However, there are also short-term risks (e.g. increased vulnerability to infection), and the long-term consequences of these treatments (e.g. the theoretical risk of malignancy) remain uncertain [56]. This is of particular concern in AS/axSpA: those who are offered biologics are often in relatively early adulthood, at a point when their disease is at its most severe and their wider lives are characterized by change and uncertainty, when they are confronted with a decision that may have profound long-term consequences.

**Shared decision-making**

Healthcare professionals play an important role as providers of information and advice for patients [57, 58]. However, treatment decisions are also influenced by interactions with people outside the healthcare team [59, 60]. In considering lay influence, the research literature focuses substantially on the significant other, often a long-term partner or spouse [61, 62]. Given that people are committing to a partner much later in life than in the past [63, 64] and a growing proportion of younger adults do not have a significant other, focusing exclusively on this relationship as a source of influence or support for decision-making is problematic.

Being clear who is involved in helping patients make healthcare decisions is important in order to ensure everyone involved has appropriate information. The healthcare
team needs to foresee challenges and pre-empt potential problems in order to tailor care and information effectively to patients’ needs.

Conclusion
The wide-ranging impact of AS/axSpA on the individual means that a holistic approach should be taken. Treating the inflammation and presuming everything else will improve is overly simplistic and runs the real risk of missing disease impact on major areas of life, with the potential to prevent patients managing and living successfully with their disease. Adopting a patient-centred approach and ensuring that the impact of AS/axSpA is considered across the physical, psychological, vocational and social spectrum, rather than maintaining a narrow focus on disease activity, should enhance care and achieve real-life improvements for patients.

Acknowledgements
Editorial assistance was provided by Succinct Medical Communications, and funded by Novartis Pharmaceuticals UK Ltd.

Supplement: Novartis has fully funded the production and printing of this supplement. Novartis suggested the topic and authors and reviewed the content to ensure compliance with appropriate regulations. Content was peer reviewed and final editorial control remained with the authors.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work on this manuscript.

Disclosure statement: J.P. has received educational honoraria from AbbVie.

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