CONCISE REPORT

Definition of disease duration in ankylosing spondylitis: reassessing the concept

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The concept and definition of disease duration in patients with ankylosing spondylitis is ambiguous, and often many years pass between the onset of symptoms and diagnosis. Members of the Assessment in Ankylosing Spondylitis (ASAS) International Working Group by consensus recently recommended identifying specific components of the medical history to better define and document the concept of disease duration. These include (1) the time of onset of the first symptoms of axial manifestations (including inflammatory back pain); (2) the time of onset of the first symptoms of each individual manifestation, which may be an extra-axial sign or symptom of ankylosing spondylitis, such as peripheral arthritis and enthesitis; (3) the time of onset of associated diseases belonging to the spondyloarthritides, in particular acute anterior uveitis, inflammatory bowel disease and psoriasis; and (4) the time since actual diagnosis by a healthcare provider. Such uniformity in data collection will ensure comparability across studies and facilitate future research.

Ankylosing spondylitis is a human leucocyte antigen-B27-associated inflammatory disease of unknown aetiology belonging to a group of diseases called the spondyloarthritides (SpA). The group represents a family of inter-related yet heterogeneous conditions with multiple clinical manifestations rather than a single disease entity.[1] Ankylosing spondylitis is the prototype of this group because of the following: (1) the existence of classification criteria; (2) improved epidemiological and clinical data; and (3) the contribution of human leucocyte antigen typing.[2] The disease predominantly affects the sacroiliac joints and axial skeleton; however, peripheral arthritis and enthesitis may also be prominent features.

In its classical presentation, ankylosing spondylitis begins with inflammatory back pain (ie, insidious onset of pain that persists for ⩾3 months, associated with morning stiffness, which improves with exercise but not with rest or inactivity). Patients with ankylosing spondylitis may also have associated conditions, including psoriasis and inflammatory bowel disease (IBD).

The pathogenic mechanisms responsible for SpA remain unknown. However, there are many shared features among the group, the most important of which include (1) negative serology for rheumatoid factor and absence of rheumatoid nodules, (2) an asymmetric oligoarthritis predominantly of the lower extremities, (3) radiological evidence of sacroiliitis and (4) familial aggregation.[1]

Ankylosing spondylitis is rarely diagnosed early, and the interval between the first symptoms and diagnosis may take, on average, 4–9 years.[3] This diagnostic delay emphasises the need for education and early recognition of the signs and symptoms of ankylosing spondylitis, particularly as effective treatments are available. The concept of disease duration and need for a consistent definition in patients with ankylosing spondylitis provided the rationale for this study.

Disease duration is difficult to conceptualise in chronic conditions where aetiology and timing of pathogenic events are unknown. However, even if these were elucidated, duration would still be difficult to ascertain on an individual level. For illustrative purposes, we borrow from another rheumatological condition—Lyme borreliosis. In this disease, cutaneous, joint, neurological or cardiac manifestations occur at different time points. The condition clearly begins with transmission of the *Borrelia burgdorferi* organism through a tick bite, which may give rise to erythema chronicum migrans. However, the inciting event (a tick bite) or rash may have gone unrecognised. Therefore, even in cases such as this where the aetiology is known, defining disease duration for a patient as the number of years after the initiating event (recognised or not) may be difficult or even impossible to determine. Analogously, inflammatory back pain may not always be the first symptom of ankylosing spondylitis. This disorder may present with enthesitis, involvement of peripheral joints or even with extra-skeletal symptoms such as acute anterior uveitis (AAU).

Alternatively, disease duration can be defined as the time since diagnosis by a healthcare provider. This approach is often used operationally for diseases such as gout, diabetes, hypertension, myocardial infarction or malignancies, although the first manifestations or organ damage may considerably antedate the time of diagnosis.

In the literature, the duration of ankylosing spondylitis has either not been defined,[4] or has been defined as years since first symptoms[3 5 6] or years since diagnosis or both.[7] Comparability across studies, including those on the efficacy of therapeutic interventions, requires standardisation in reporting disease duration. Our article aimed to provide recommendations to promote uniformity in data collection to ensure comparability across studies and facilitate future research endeavours.

METHODS

The Assessment in Ankylosing Spondylitis (ASAS) International Working Group comprises experts in the field of ankylosing spondylitis working to improve multiple research tools in the specialty, including defining the concept of disease duration. At the annual ASAS meeting (January 2005 in Amsterdam, The Netherlands), results of a web-based questionnaire on opinions pertaining to the reporting of the disease onset or duration were presented. This questionnaire was completed online by 31 of the 38 (82%) ASAS members before the meeting. A detailed consensus-building discussion ensued, which included (1) a review of

Abbreviations: AAU, acute anterior uveitis; ASAS, Assessment in Ankylosing Spondylitis; IBD, inflammatory bowel disease; SpA, spondyloarthritides

Box 1 ASAS consensus on ankylosing spondylitis (AS)-specific and AS non-specific components

AS-specific

- Axial or sacroliac joint symptoms including inflammatory back pain
- Peripheral arthritis
- Enthesitis (eg, Achilles tendonitis)

Non-AS-specific

- Acute anterior uveitis
- Inflammatory bowel disease
- Psoriasis

the responses to the questions, followed by (2) general discussion and (3) final voting on each concept (http://www.asas-group.org/phpQ/stats.php?sid = 27&-st = a&vw = a). The results and final consensus are reported here.

RESULTS

Only 7% of the participants believed that duration of disease should imply only the time (years) since diagnosis by a healthcare provider; 45% thought this should imply time since onset of the first symptom, whereas the remaining 48% indicated that the term was ambiguous and should indicate both the time since diagnosis and the time since the first symptom. Nearly all the participants (97%) stated that this issue is crucial and should be clarified, uniformly applied and studied further.

The next item considered was the issue of perceived accuracy in reporting of the first symptom. Although no one believed that this assessment would be accurate in every case, most of them (74%) considered this to be useful and worthy of ascertainment. In addition, we asked whether manifestations such as a first episode of AAU, preceding IBD, psoriasis or peripheral arthritis, or tendonitis preceding axial manifestations of ankylosing spondylitis should qualify as the first ankylosing spondylitis-specific symptoms. It was believed that preceding ankylosing spondylitis-specific manifestations should apply to peripheral arthritis (87%) and enthesitis (eg, Achilles tendonitis, 71%), but not to AAU (32%), Crohn's disease (19%) or psoriasis (16%; box 1).

Although 48% stated that it would be preferable to report years since onset of first symptoms or manifestation, most of them (52%) emphasised that both years since onset and years since diagnosis should be provided when data for research are collected.

The following essential items were therefore recommended in the collection and reporting of data on disease duration in patients with ankylosing spondylitis (box 2): (1) the time of onset of the first symptoms of axial manifestations (ankylosing spondylitis-specific, including inflammatory back pain); (2) the time of onset of the first symptoms of each individual manifestation that may be an extra-axial sign or symptom of ankylosing spondylitis, such as peripheral arthritis, enthesitis or other extra-articular manifestations; (3) the time of onset of associated diseases belonging to SpA, in particular AAU, IBD and psoriasis; and (4) the time since actual diagnosis by a healthcare provider.

DISCUSSION

In dealing with studies or patient populations, the aim should be to make communication more uniform about what constitutes the beginning of the disease.

Box 2 Defining disease duration: components for data collection

- Onset of axial ankylosing spondylitis (AS)-specific manifestations (inflammatory back pain)
- Onset of extra-axial AS-specific manifestations spondyloarthritides (peripheral arthritis, enthesitis)
- Onset of associated spondyloarthritides diseases (acute anterior uveitis, inflammatory bowel disease, psoriasis)
- Time since diagnosis of AS by a healthcare provider

The last item of the recommendations—that is, time since diagnosis of ankylosing spondylitis—may not be useful clinically, given the delay in diagnosis in most patients, but will aid in issues related to regulation, research and education.

Clearly, several questions remain to be answered. One is the issue of disease beginning with the onset of chronic disease versus relapsing symptoms, and specifically how this should be differentiated from single or multiple flares. That there may be a long time interval between the occurrence of flares is also acknowledged. It was also believed that distinctions should be made on whether the symptoms are transient (lasting only days to weeks) or continuous (lasting >3 months as per the modified New York criteria for ankylosing spondylitis).

In addition, time to first symptom that was non-axial versus first axial-related back pain symptom was discussed in more detail (see items 1–3 later). Clearly, assessing disease duration by studying patient histories from medical records may lack accuracy because of missed or inappropriate diagnosis. This might be true for a patient's recall of symptoms as well. Recollection is more accurate if a patient has been diagnosed recently. Zink *et al*[8] examined age at onset of multiple diseases with diagnosis of <5 years and indeed patient recall was better in those with more recent diagnoses.

Apart from clinical studies, particular applications of this proposal include (1) research on clinical care over time, focusing on narrowing the time between the onset of symptoms and diagnosis; (2) studies on whether the onset of certain manifestations of spondyloarthritis, or non-axial or peripheral joint symptoms have prognostic implications; and (3) the assessment of the average duration of time between manifestations. Peripheral arthritis, enthesitis and dactylitis were perceived as spondyloarthritic, peripheral or extra-axial manifestations of ankylosing spondylitis, whereas the first symptoms of IBD, AAU or psoriasis were not considered as the first signs of ankylosing spondylitis, but as expressions of associated disease. Participants, however, thought it important to capture peripheral and other extra-axial symptoms, but also the associated SpA, AAU, IBD and psoriasis. The underlying idea is that these diseases might influence one or more aspects of ankylosing spondylitis, such as aetiology, pathogenesis, or signs and symptoms.

In conclusion, the definition of disease duration in patients with ankylosing spondylitis is at best ambiguous. Important components of the recommendations to better define duration of disease were found to be (1) time of onset of ankylosing spondylitis-specific symptoms (inflammatory back pain); (2) onset of signs of spondyloarthritis, peripheral or extra-axial symptoms; (3) onset of associated SpAs; and (4) time of diagnosis of ankylosing spondylitis by a healthcare provider. Such uniformity in data collection will enable better comparability across studies about the efficacy of interventions and facilitate answering important research initiatives.

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