Assessment of ankylosing spondylitis

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ABSTRACT

Outcome measures for the assessment of patients with ankylosing spondylitis (AS) have been the subject of considerable research in the last decade, largely through the contributions of the ASessments in Ankylosing Spondylitis (ASAS) International Working Group. This review focuses on the measurement of disease activity, physical function and structural damage in AS, both in daily patient care and to measure treatment response in clinical trials. The ASAS Core Sets for assessment in AS are an important tool to guide disease monitoring, and the domains they contain are discussed, along with other possible concepts important to patient care, including imaging and health-related quality of life. In clinical trials, the assessment of disease response to therapy using the ASAS Response Criteria is a valuable means of determining treatment efficacy and allows comparison of response across trials and interventions.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatological disease characterized by spinal inflammation, usually in the form of sacroiliitis and spondylitis which may lead to syndesmophyte formation and ankylosis in the further course of the disease. AS most commonly begins in the second and third decade of life as persistent inflammatory back pain that can already be associated with significant loss of function, work disability and impaired quality of life early in the disease (1-3). There is a well-recognized delay in diagnosis of up to 7 years (4) which necessitates an early high level of suspicion in young patients presenting with inflammatory back pain at the primary care level.

When assessing patients with AS, it is useful to think of measuring disease activity, physical function and structural damage as separate facets of the AS process: disease activity reflects acute inflammation and rate of change, physical function reflects the impact the disease has on the patient's ability to perform activities in his/her daily life, and structural damage reflects the end result of the AS process on anatomical structures. Measurement tools for AS may assess 1, 2 or all 3 of these domains (Table I).

The ASessments in Ankylosing Spondylitis (ASAS) group is an international collaboration of clinicians, researchers and industry representatives with a particular interest and expertise in AS. ASAS was established in 1995 with a goal to improve the assessment of this debilitating disease. The group has developed practical, concise core sets of concepts important for patient monitoring (Table II), both in a clinical practice setting and for assessing treatment response in clinical trials (5).

The core sets were created using a combination of expert consensus, research evidence and statistical approaches, and can be thought of as a standard framework for patient assessment. ASAS has subsequently reviewed the extensive literature on different outcome measures and instruments which have been used in AS clinical trials, and selected the most appropriate measures for each core set domain based on evidence of validity and consensus opinion (6). Assessment of the validity, reliability and responsiveness of the recommended measures in interventional trials is ongoing (7).

The ASAS group recommends that the measures put forward in the core sets be used in all research projects in AS to standardize outcome measurement, to ensure that meaningful patient outcomes are not overlooked, and to facilitate comparisons of response across studies. It is emphasized that although the core sets describe the minimum set of domains that should be assessed and monitored in AS patients, they are not exclusive or exhaustive; other concepts such as health-related quality of life can also add important information,

and each situation should be assessed individually with regard to the specific aim of the assessment.

Finally, it must be recognized that core sets perform according to the task they were designed to meet. Thus, core sets for clinical studies may differ from measurements for individual patient care. The ASAS core set for clinical record keeping is recommended for use in daily practice by the recently developed ASAS/EULAR evidence-based recommendations for the management of AS (8, 9)

Table I.

Domain	Disease activity	Function	Damage
Patient global assessment	x	x	x
Spinal pain	x		x
Spinal stiffness	x	x	x
Spinal mobility	x	x	x
Physical function	x	x	x
Peripheral joints and entheses	x	x	
Fatigue	x		
Disease activity	x		
Quality of life	x	x	x
Acute phase reactants	x		
Imaging	x		x

Table II. ASAS core sets for assessment in ankylosing spondylitis.

Domain	Core set			Instruments
	CR	SMARD/PT	DC-ART	
Patient global assessment	x	x	x	VAS in the last week
Spinal pain	x	x	x	VAS pain at night, average in the last week, and VAS, average in the last week
Spinal stiffness	x	x	x	VAS morning stiffness
Spinal mobility	x	x	x	Chest expansion, modified Schober index, and occiput-to-wall distance
Physical function	x	x	x	Bath Ankylosing Spondylitis Functional Index, or Dougados Functional Index
Peripheral joints and entheses	x		x	Number of swollen joints; no preferred instrument for entheseal disease
Fatigue			x	No preferred instrument
Acute phase reactants	x		x	ESR
Imaging			x	APand lateral x-rays lumbar spine, lateral cervical spine, pelvis (SI and hip joints)

CR: clinical record keeping; DC-ART: disease-controlling anti-rheumatic therapy; SMARD: symptom-modifying anti-rheumatic drugs; PT: physical therapy.
VAS: Visual analogue scale; ESR: Erythrocyte sedimentation rate; AP: antero-posterior; SI; sacroiliac.

Patient global assessment

The impact of AS from the patient perspective encompasses all aspects of disease including activity, function and structural damage, in one summary measure. The ASAS group recommends the use of a single visual analogue scale measure (VAS) of global well-being "on average over the last week" as an important component of the clinical assessment. This is consistent with the other measures in the core set, utilizing the 'in the last week' approach to obtain a snapshot of current patient status. The patient global assessment is useful in clinical practice, and may be the single most responsive measure in this setting. An alternative global measure, the Bath Ankylosing Spondylitis Global score (BAS-G) (10) combines two VAS scores, one referring to the last week and the second to the patient's average well-being over the last 6 months, which can be helpful to describe longer-term disease progression.

Spinal pain

Inflammatory back pain can be considered the cardinal symptom of AS (11), and has a sensitivity and specificity of 75% for the diagnosis of axial disease (12). Available measures of spinal pain cannot distinguish accurately between the pain of inflammation and mechanical back pain due to structural damage however. The ASAS core sets consider nocturnal spinal pain due to AS on average over the past week, reflecting largely inflammatory pain, and spinal pain due to AS on average over the past week at any time to be the most useful for monitoring disease. For initial patient assessment, it is also useful to ask specifically about the severity of spinal pain at its worst and its best, the duration of spinal pain throughout the day, and its response to exercise and rest. Pain severity can be evaluated using a qualitative approach ('mild', 'moderate' or 'severe'), but it is often more useful to measure pain on either a numerical rating scale (0-10, where 0 = 'no pain' and 10 = 'unbearable pain') or a VAS, as used in the ASAS core sets (0-100 mm, where 0 = 'no pain'and 100 = 'unbearable pain'). This scale gives a better indication to the clinician of how pain is affecting the patient in daily life, and is a quantifiable baseline against which future pain can be measured.

Spinal stiffness

Spinal stiffness refers to morning stiffness, a symptom of inflammation reflecting disease activity and impacting on physical function. Structural damage, in particular the presence of syndesmophytes and ankylosis, results in a static spinal stiffness which does not

change over the course of the day. The duration of morning stiffness from the time of awakening is a simple means to quantify inflammatory symptoms; the ASAS group proposes that the overall level of morning stiffness over the past week is also important, and that together these two measures perform better than measuring duration of stiffness alone. Change in the duration of morning stiffness can be interpreted as a change in inflammation, as structural damage does not change over this time frame.

Table III. Clinical examination of spinal mobility.

Measure	Description
Cervical mobility	
Occiput-to-wall distance*	Horizontal distance between occiput and wall, patient standing with heels and buttocks against the wall.
Tragus-to-wall distance	Horizontal distance between right tragus and wall, patient standing with heels and buttocks against the wall without rotation.
Cervical rotation	Distance between tip of nose and acromioclavicular joint in neutral less the same distance in maximal ipsilateral rotation.
Thoracic mobility	
Chest expansion*	The difference in centimetres to the nearest 0.1 cm between full expiration and full inspiration, measured at the nipples.
Lumbar mobility	
Modified Schober index*	Distance between the midpoint of the posterior superior iliac spines and a point 10cm vertically above when standing erect, following maximal forward flexion of the spine (normal > 15cm)
Finger-to-floor distance	Distance between tip of middle finger and the floor following maximal lumbar forward flexion with knees extended
Lumbar lateral flexion	Distance between tip of ipsilateral middle finger and the floor following maximal lumbar lateral flexion, with both feet on the floor, knees extended and without rotation

*Recommended in the ASAS Core Sets.

Spinal mobility

Spinal mobility can be impaired by acute spinal or sacroiliac inflammation, or by the formation of syndesmophytes, intervertebral bridging and ankylosis. There are numerous examination techniques for measuring the different facets of spinal mobility, which are reliable and valid but vary in their responsiveness to change (13). At a minimum, flexibility of the cervical and thoraco-lumbar spine and chest expansion should be assessed. Some of the more commonly used measures are given in Table III. The ASAS Core Sets recommend the modified Schober's test to measure thoraco-lumbar mobility, and the occiput-to-wall distance to measure mobility of the cervical spine. The Bath Ankylosing Spondylitis Metrology Index (BASMI) combines spinal mobility and hip function into a composite index, consisting of tragus-to-wall, lumbar flexion, cervical rotation, lumbar lateral flexion and intermalleolar distance (14).

Physical function

There is no single parameter that adequately measures the concept of physical function. A number of patient-assessed AS-specific instruments are available which cover a range of physical functions and activities of daily living, in order to summarize how a well a patient functions in daily life and to quantify 'disability' (Table IV). The most commonly used are the Bath Ankylosing Spondylitis Functional Index (BASFI, Table III) (15) and the Dougados Functional Index (DFI) (14). Both have been shown to perform well with regard to reliability, validity and responsiveness across a range of settings (17,18), although the DFI may not be as responsive to small changes as the BASFI due to skewed score distribution and a floor effect (19). Other instruments measuring physical function in AS patients, including the Ankylosing Spondylitis Assessment Questionnaire (ASAQ) (20), the modified Health Assessment Questionnaire for the spondyloarthropathies (HAQ-S) (21) and the Revised Leeds Disability Questionnaire (RLDQ) (22) have not been as extensively validated in clinical trials and cannot be recommended over the BASFI or the DFI at this time.

Peripheral joints and entheses

Peripheral joint involvement occurs in approximately 25% of patients with AS, usually in the form of oligo-articular, asymmetrical large joint involvement. The formal joint counts in use for rheumatoid arthritis are therefore not necessarily useful in this setting. The ASAS group suggests using a 44-joint count, which includes the sternoclavicular joints, acromioclavicular joints, shoulders, elbows, wrists, knees, ankles, metacarpophalangeal and metatarsophalangeal joints, and the proximal interphalangeal joints of the hands. The core set advocates measuring only swollen joints in this way; arguments can be made for recording tender or painful joints also. Peripheral joint disease reflects both disease activity (acute inflammation) and physical function, but rarely progresses to significant structural damage. Hip involvement may result in marked joint destruction, but is generally classified as axial, not peripheral, disease.

There is no specific instrument recommended in the ASAS core sets for the assessment of enthesitis in AS. The Mander Enthesitis Index (MEI) was the first composite measure designed to evaluate enthesitis in AS patients, assessing 66 different entheses for tenderness, rated by the intensity of pain on compression (0 = no pain, 1 = mild pain, 2 = moderate pain and 3 = winces or withdraws) (23). The MEI is time-consuming to complete, and it is not clear if a low score reflects clinically important disease. A simplified enthesis count has since been developed, and validated against the MEI and disease activity.

The Maastrict Ankylosing Spondylitis Enthesitis Score (MASES) includes only 13 entheses, and uses the dichotomous responses 'no pain'and 'painful' for each site, resulting in a score be-

Table IV. Validated disease-specific instruments used for measurement in ankylosing spondylitis.

Instrument	Abbrev.	Measures	Description
Bath Ankylosing Spondylitis Disease Activity Index (31)	BASDAI	Disease activity	Acomposite index made up of 6 questions, each measured on a 0-100mm visual analogue scale (VAS): - fatigue - neck, back or hip pain - pain/swelling in other joints (not neck, back or hip) - overall discomfort from tender areas - overall level of morning stiffness (intensity) - duration of morning stiffness
Bath Ankylosing Spondylitis Functional Index (15)	BASFI	Function	Acomposite index made up of 10 questions, covering basic daily functions such as bending and standing, each measured on a 0-100mm VAS
Dougados Functional Index (16)	DFI	Function	Acomposite index made up of 20 questions, covering basic daily functions such as bending and standing, using the categorical response options 'yes, with no difficulty'. 'yes, but with difficulty'and 'no'.
Bath Ankylosing Spondylitis Metrology Index (14)	BASMI	Function (spine and hip)	Acomposite index made up of 5 clinical measurements: - cervical rotation - tragus to wall distance - lumbar side flexion - modified Schober's test - intermalleolar distance
Bath Ankylosing Spondylitis Radiology Index (59)	BASRI	Structural damage	X-ray scoring system for the lateral cervical spine, APand lateral lumbar spine and hips, using the New York system to grade the sacroiliac joints.
Modified Stoke ASSpinal Score (58)	mSASSS	Structural damage	X-ray scoring system for the lateral cervical and lateral lumbar spine, score range 0-72

tween 0 and 13 (24). It is therefore easier to administer than the MEI, although it may not be as sensitive at the lower end of the scale. Further validation of the MASES in clinical trials will be required to answer this question. Another simplified enthesitis score has been developed in Berlin which requires the assessment of 12 different entheses for disease involvement and is expressed as a simple score between 0 and 12 (25); this method has not yet been formally validated.

Fatigue

Fatigue is an important source of morbidity in AS patients (26), associated with disease activity, functional ability and global well-being (27, 28). There are no specific disease-related measurement instruments for fatigue in AS. One question in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) asks about the overall level of fatigue/tiredness in the past week (VAS, 0-100 mm), but none of the other composite instruments address this domain. This item has recently been shown to be sensitive and specific for fatigue in AS patients with a cut-off of 70 mm (28), and is the recommended instrument for measuring fatigue in the ASAS core sets. Many validated fatigue questionnaires specific to other diseases are available, but these were not thought to be relevant to AS patients by the ASAS group. The general Multidimensional Fatigue Inventory (MFI) (29) gives insight into different aspects of fatigue, and preliminary validation studies in AS are encouraging (30).

Disease activity

Disease activity in AS is measured by the BASDAI (31), a composite index that evaluates fatigue, axial and peripheral pain, stiffness and enthesopathy (Table IV). The self-administered instrument is made up of 6 questions regarding the patient's symptoms in the previous week, each to be answered on a VAS scale (0-10 cm), where 0 = none (or 0 hours for morning stiffness) and 10 cm= very severe (or 2 or more hours for morning stiffness). The BASDAI is easy and quick to complete, the final score is a simple sum of its components, and has been extensively validated in clinical trials (18, 32) and translated into several languages. A BASDAI score > 4 is internationally accepted to indicate active disease, and most clinical trials of therapy in AS now require that patients have active disease as defined by a BASDAI >4 for inclusion. The BASDAI is one of the most commonly used outcome measures in clinical trials, and is simple enough to be implemented in daily practice.

Health-related quality of life

The measurement of health-related quality of life is not included in the ASAS core sets, but is worthy of consideration as a component of patient assessment, as it incorporates all three facets of disease – activity, function, and damage. There are now validated AS-specific instruments to measure disease-related quality of life. The most thoroughly studied is the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire (33), an 18-item scale with dichotomous responses (yes/no), which is reliable and valid for measuring health-related quality of life in AS

patients. The ASQoL is easy to administer and correlates well with the well established generic EuroQol (34), but has been criticized for omitting important patient factors such as body image and walking (18). It has been shown to be responsive in clinical trials of anti-TNF-α therapy (35), but less useful to measure changes after physical therapy or standard care (36, 37).

The ankylosing spondylitis Arthritis Impact Measurement Scales 2 (AS-AIMS) (38) consists of 63 items using a 5-point categorical scale for each response, which allows a more detailed measurement of patient health than dichotomous responses. Another AS-specific measure of health-related quality of life is the Patient Generated Index (PGI) (39), an individualized measure in which patients are asked to list the most important areas of their lives which are affected by AS, and then to rank and score them, resulting in a single index of AS-specific quality of life. The properties of these two instruments have been less carefully studied than the ASQoL, and therefore at this time it is not possible to compare the respective merits of the different instruments.

Other arthritis-specific instruments have been used to assess quality of life in AS studies. The original Arthritis Impact Measurement Scales (AIMS, AIMS2) (40, 41) have 45 and 57 items respectively, each with categorical response options, and the Patient Elicitation Technique (PET) is a single index with 15 items and descriptive responses (42, 43). These instruments have been widely used in RA, but have not been investigated for reliability or discrimination in AS, and only limited evidence for validity or responsiveness is available. However, they may be more appropriate than disease-specific measures when comparing health-related quality of life between patients with AS and patients with other rheumatological conditions.

Generic health measures

Most generic health measures are about 50% as responsive as disease-specific measures (44), reflecting the trade-off for their generalisability over different disease states, and therefore have limited application in daily clinical practice. Nevertheless, these instruments can be valuable in research settings in the absence of corresponding AS-specific measures or for comparing health states across diseases.

The Medical Outcomes Study Short Form 36 (SF-36) (45) and the EuroQol (34) have both been validated as measures of health-related quality of life in AS patients (46). The SF-12 Physical Component Summary Scale appears to be the most appropriate subscale for measuring routine practice and clinical research. The Stanford Health Assessment Questionnaire (HAQ) (47) has been less thoroughly studied in AS, and is largely superceded by the HAQ-S in this population. Disability, a multi-dimensional construct uniting problems at the physical, personal and social levels, can be assessed using the World Health Organization Disability Assessment Schedule II (WHODAS II), validated in AS patients (48). The concepts within this instrument are consistent with the WHO International Classification of Functioning, Disability and Health (ICF) (49), and work is ongoing to develop disease-specific ICF Core Sets relevant to AS. The comparison of health across disease states is not straightforward; although a generalizable instrument is essential, there have been concerns that even these are not as valid as was commonly thought, since patients with different diseases will interpret the same questions differently (i.e., from a different frame of reference) (50).

Acute phase reactants

Laboratory investigations in AS should include the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) as a measure of inflammation (an indicator of disease activity). Although neither measure is diagnostic for AS (up to 40% of AS patients never exhibit raised acute phase reactants despite their having active disease) and CRP has not proved useful for detecting short-term change in axial disease in NSAID trials (51), acute phase reactants are likely to be raised in patients who have peripheral joint involvement or significant extra-articular disease such as inflammatory bowel disease (52). Neither measure is superior for disease assessment in AS (53, 54); the ESR has been chosen as the preferred reactant in the core sets for reasons of cost and availability.

Imaging

Imaging structural damage in AS is still under evaluation. Radiography is the conventional imaging modality used in AS, but other techniques are being used with increasing frequency to assess different aspects of the disease process.

Plain radiographs

In addition to clinical features, the modified New York criteria for the diagnosis of AS (Table V) require evidence of sacroiliitis on plain x-ray (55). The ASAS core sets recommend plain x-ray of the pelvis to view the sacroiliac joints, because this includes both the sacroiliac joints and the hips, is not inferior to specific sacroiliac views (56), and minimizes exposure to irradiation.

Structural changes of AS, including syndesmophytes, erosions, sclerosis and ankylosis, can be seen on spinal x-ray. Plain x-rays of the spine should include AP and lateral views of the lumbar spine and lateral views of the cervical spine. There are currently three validated scoring systems used to assess spinal structural damage in clinical trials in AS: the original Stoke Ankylosing Spondylitis Spinal Score (SASSS) (57), a modified SASSS (mSASSS) (58), and the Bath Ankylosing Spondylitis Radiographic Index (BASRI) (59) (Table IV). The SASSS and the BASRI are not sensitive to change over periods of 1 to 2 years (60, 61), possibly due to the relatively slow progression of disease in many patients with AS. The mSASSS performs better, having been shown to detect changes over 24 months in population studies (62, 63).

Computed tomography (CT)

CT is more sensitive than plain x-ray for detecting bony changes secondary to sacroiliitis, and the cross-sectional images allow a more complete image of the anatomy of the sacroiliac joints. It appears to be the best method to detect and diagnose early bone chan-

Table V. Modified New York Criteria for AS (1984).

Criteria	Description
Clinical criteria	(a) Low back pain and stiffness for more than 3 months which improves with exercise, but is not relieved by rest (b) Limitation of motion of the lumbar spine in both the sagittal and frontal planes (c) Limitation of chest expansion relative to normal values correlated for age and sex
Radiological criterion	Sacroiliitis grade ≥ 2 bilaterally or grade 3-4 unilaterally – Grade 0 = normal – Grade 1 = suspicious – Grade 2 = sclerosis, some erosions – Grade 3 = severe erosions, widening of the joint space, some ankylosis – Grade 4 = complete ankylosis

Definite AS is present if the radiological criterion is associated with at least 1 clinical criterion (55)

ges, such as erosions and regional ankylosis, which may not be visible on plain x-ray (64). However, sacroiliac sclerosis, joint space narrowing and erosions can also be a part of the normal aging process (65), and CT can therefore give a false positive diagnosis of sacroiliitis.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) of the sacroiliac joints and the spine is increasingly used to assess disease activity in AS. Although MRI has not been incorporated in the ASAS core set to date, it appears likely on the basis of recent data that MRI will play a role both in clinical trials and in the standard care of patients, because it is advantageous to have objective evidence of spinal inflammation.

While conventional radiography of the spine and sacroiliac joints is used primarily to detect chronic structural changes in AS, MRI is indicated to detect active axial inflammation, including sacroiliitis, spondylitis and spondylodiscitis (66-68), which are not clearly visible with other imaging techniques. Reported MRI abnormalities correspond to acute inflammatory processes within both the bone and the sacroiliac joint (69, 70). Although all three spinal segments are affected by spinal inflammation, active spinal changes are most frequently identified in the lower part of the thoracic spine (71). T1-weighted MRI is also able to detect chronic changes, particularly in the thoracic spine, which is poorly visualized with other methods (72). To quantify acute and chronic spinal changes in clinical trials, a new MRI scoring system (ASspiMRI) has been developed and validated (64, 73, 74). Vertebral units are scored for changes of active disease (0-6) and chronic changes (0-6). The ASspiMRI may be used to identify AS patients with active disease, and is sensitive to detect change with anti-TNF therapy in clinical trials.

Ultrasound

Ultrasonography can be useful to detect enthesitis and bursitis in patients with spondyloarthritides (75, 76). Ultrasound is much more sensitive than clinical examination for detecting these changes, and in clinical practice can assist in diagnosis, as well as in treatment with ultrasound-directed aspiration and/or corticosteroid injection. A scoring system for measuring enthesitis by ultrasound in clinical trials has been proposed, but is not yet validated (75).

Dual energy x-ray absorptiometry (DEXA)

Osteoporosis is commonly associated with AS, particularly in patients with syndesmophytes (77), and the resultant vertebral fractures can contribute to spinal pain, stiffness and loss of mobility (78). Dual energy x-ray absorptiometry (DEXA) of the hip and antero-posterior lumbar spine is the most frequently used method for assessing bone mineral density (BMD) in post-menopausal women. In AS patients, DEXA of the lumbar spine can give a falsely elevated BMD value as a result of co-existent syndesmophyte formation (77). The use of lateral lumbar spine DEXA may be a better method to measure spinal BMD in AS patients (79). DEXA has been shown to be sensitive to improvement in BMD at the lumbar spine and the hip in AS patients treated with infliximab over 6 months (80). Dual energy quantitative computed tomography (DEQCT), peripheral QCT, and calcaneal quantitative ultrasound (QUS) have been used in clinical trials to assess bone loss in AS, but their usefulness in daily clinical practice has not been established.

Measuring treatment response

New therapies for AS over the last 5 years have improved treatment options and patient outcomes (81), but we need to be able to measure treatment effects in clinical trials to allow the objective evaluation of therapies and subsequently rational treatment choices in daily patient care. The ASAS group has taken the core sets and their respective measurement instruments to construct specific composite response criteria for use in measuring the treatment response in AS trials (Table VI). Derived from 5 short-term trials of NSAIDs in AS, the initial improvement criteria consist of four outcome domains: physical function, spinal pain, patient global assessment and inflammation (82). Improvement is defined as a 20% improvement from baseline, or a 10 mm improvement from baseline for VAS measures on a 0-100 mm scale, in at least 3 of the 4 domains. There cannot be deterioration of 20% or more, or of 10 mm or more on a VAS scale, in the corresponding 4th domain. The response criteria show high specificity and moderate sensitivity (83), and have been validated in studies of anti-TNF-alpha therapy (84). These are now termed the ASAS 20% response criteria (ASAS20), and allow the calculation of treatment response as a dichotomous variable, 'responder' and 'non-responder', and subsequent calculation of the number needed to treat (NNT) for interventions in AS.

Further investigation of the response criteria has introduced variations in the ASAS-IC which appear to perform better in defining the treatment response,

Table VI. ASAS response criteria.

Instrument	Abbrev.	Description
ASAS improvement criteria (81)	ASAS-IC	Four domains, based on the discrimination between NSAID treatment and placebo - Physical function, measured by the BASFI - Spinal pain, measured on a 0-100mm VAS - Patient global assessment in the last week, on a 0-100mm VAS - Inflammation, measured as the mean of the last 2 BASDAI questions (intensity and duration of morning stiffness)
ASAS 20% response criteria (81)	ASAS20	Treatment response is defined as: - ≥ 20% and ≥10mm VAS on a 0-100 scale in at least 3 of the 4 ASAS-IC domains, and - No worsening of ≥ 20% and ≥ 10mm VAS on a 0-100 scale in the remaining 4th domain
ASAS 40% response criteria (84)	ASAS40	Treatment response is defined as: - ≥40% and ≥20mm VAS on a 0-100 scale in at least 3 of the 4 ASAS-IC domains, and - No worsening of ≥40% and ≥20mm VAS on a 0-100 scale in the remaining 4th domain
ASAS 5 out of 6 response criteria (84)	ASAS 5/6	Developed for use in trials of anti-TNF therapy, six domains were included: - Pain - Patient global assessment - Function - Inflammation - Spinal mobility - C reactive protein (acute phase reactant) Treatment response is defined as improvement in 5 of 6 domains without deterioration in the 6th domain, using predefined % improvements.

specifically in anti-TNF-alpha studies (85). Raising the cut-off for defining improvement from ≥ 20% to ≥ 40%, and from ≥ 10mm to ≥ 20mm for the VAS scales, in 3 of the 4 domains (with no deterioration of ≥ 40% or of ≥ 20mm VAS in the 4th domain) (ASAS40) improved the performance of the response criteria in this setting, with a low placebo response rate and high response to infliximab treatment. The '20% improvement in 5 of 6 domains' instrument was equally responsive and discriminative. Further validation of these new modifications to the response criteria is ongoing.

In 2003, the ASAS group published an international consensus statement for the use of anti-TNF-alpha agents in clinical practice in patients with AS (86), and a recent update of the same (87). These statements suggest that both the ASAS core set for clinical practice and the BASDAI should be used to monitor patients receiving anti-TNF-alpha therapy. Response to therapy in clinical practice is defined as improvement of at least 50% or 2 units on a 0-10 scale of the BASDAI, and expert opinion that treatment should be continued. If this response is not achieved after 6-12 weeks of therapy, discontinuation of treatment should be considered.

Conclusion

The ASAS Core Sets, their recommended measurement instruments and the ASAS Response Criteria represent a significant advance in the assessment of ankylosing spondylitis. We now have an evidence-based approach to patient assessment, both for measuring patient response to therapy in clinical trials and for monitoring disease activity, physical function and structural damage in daily patient care. Critical evaluation of this approach is ongoing, particularly with regard to the assessment of disease severity, the role of MRI, and health-related quality of life measurement.

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