Patientreported outcomes in ankylosing spondylitis: development and validation of a new questionnaire for functional impairment and quality of life assessment

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Abstract

Objectives

To assess validity, reliability and sensitivity to change of a new questionnaire for assessment of functional disability and quality of life in ankylosing spondylitis (AS) patients.

Methods

Using Rasch analysis and 71 questions item pool, content analysis and semi structured group discussion, the combined AS questionnaire (CASQ) was developed including: 10-item scale to assess functional impairment (CASQ-FI), and 10 items to assess quality of life (CASQ-QoL). Construct validity was assessed by correlating the score of the questionnaire to parameters of disease activity namely, the BAS-FI, BAS-DAI, BAS-G, BAS-Metrology Index, and the occupational status. In addition, the CASQ was compared to both HAQS and ASQoL. Sensitivity to change of the developed CASQ was also assessed.

Results

The CASQ questionnaire for functional impairment (CASQ-FI: 10 items) and quality of life (CASQ-QoL: 10 items)showed acceptable validity as it correlated significantly with clinical parameters of disease activity: BAS-FI (CASQ-FI: r=0.85, CASQ-QoL: r=0.86), BAS-DAI (CASQ-FI: r=0.71, CASQ-QoL: r=0.87) and BAS-G (CASQ-FI: r=0.64, CASQ-QoL: r=0.79). Compared to HAQS and ASQoL, the CASQ-QoL was as well or better correlated with clinical and outcome measures. The CASQ was also reliable (Cronbach's alpha for CASQ-FI 0.958, and CASQ-QoL 0.966) and had no misfitting items. In addition, both CASQ questionnaires were sensitive to change ($p<0.01$)

Conclusions

The CASQ is a reliable and valid tool for assessment of functional impairment and quality of life in AS. The CASQ is well accepted by patients, sensitive to change, easy to administer and score. The CASQ-FI and CASQ-QoL questionnaires can either be used and scored separately to assess for functional disability as well as quality of life or in combination as tools to assess for both parameters.

Key words

ankylosing spondylitis, AS, CASQ, functional impairment, quality of life

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Received on September 19, 2010; accepted in revised form on May 20, 2011.

Competing interests: none declared.

Introduction

Ankylosing spondylitis (AS) is a chronic, often progressive, inflammatory disorder, primarily affecting the sacroiliac joints, the axial skeleton and thoracic cage (1). Patient-assessed instruments become increasingly important in the measurement of health outcomes in rheumatology and provide supplementary information to traditional biomedical assessment. When determining the effect of disease on a patient, information can be collected on impairments (symptoms and well-being), disability and handicapping (functioning), as well as quality of life (2, 3). The WHO, international classification of functioning, disability and health (ICF), recommended that future functional and disability assessments are likely to get more sophisticated as the interaction among illness, functional disability, psychological status and society interaction become increasingly recognised (4). A recent study highlighted also that functional limitation is a modifiable outcome of disease, and provides a measure of progress in developing and disseminating effective treatments (5). Among AS patients, while measures of impairment and activity limitation are used to determine disease severity and identify the need for changes in treatment (this includes Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis-Functional Index (BASFI), Dougados Functional Index (DFI), Health Assessment Questionnaire for Spondyloarthritis (HAQS), and Leeds Disability Questionnaire); quality of life measures are intended to determine the holistic impact of the disease and its treatment from the patients' perspective (*e.g.* Ankylosing Spondylitis Quality of Life (ASQoL), Short Form-36 (SF-36) and Euro-QoL) (6, 7).

The challenge in HRQoL measurement is its multidimensional nature, which takes into account not only how a person functions physically, mentally and socially, but also incorporates an evaluative component that assesses a person's satisfaction with his or her current health status (8). The Assessment in Ankylosing Spondylitis Group (ASAS) has recommended several domains for the evaluation of patients with AS in both clinical research and routine practice (9-12), which included the assessment of activity limitation (BASFI), disease activity (BASDAI) as well as patient's global of disease activity (BASG) (13, 14).

In this work, we developed and validated a new questionnaire which assesses functional disability as well as quality of life separately among patients suffering from AS. This study addressed also the sensitivity to change of this newly developed tool.

Patients and methods

This was a multicentre study aiming at developing two questionnaires for assessment of (1) functional disability and (2) quality of life using an item bank and Rasch analysis (15). All patients included in this work met the modified New York criteria for AS (16). The sample included patients with both axial and peripheral disease, a range of disease duration as well as extra-articular manifestations. All the patients included in the study were recruited from those recorded on the rheumatology department records.

Step I: Development of an AS specific item pool

After reviewing the literature, a random sample of 102 patients (90 males, 12 females; mean age 40.2±9.72 years, mean disease duration 12.1±5.43 years) were interviewed to identify the effect of AS on their daily living. Eleven patients did not wish to participate in the interviews for work commitment, however they were happy to be included in the validation protocol. All patients met the modified New York criteria for AS. Data were recorded using a structured proforma sheet. Interviews took place in a private room and lasted between 30–60 minutes. The patients were given the opportunity to identify areas of their lives that were important from their point of view. Following a content analysis of the transcripts reflecting important patient-reported outcomes, the AS-specific measures of impairment and health related quality of life were listed. Related themes were highlighted, grouped together and organised

by conceptual categories (17-19). The content analysis and category identification was discussed between members of the development team and assessed for repetition and ambiguity. In total, 71 items were identified including 42 items expressing functional impairment and 29 items for quality of life.

Step II: Development of the questionnaire

172 registered patients (146 males, 26 females, mean age 39.4±8.9 years, mean disease duration 11.6±4.5 years) who meet the modified New York criteria for AS were included in this step of the work. Patients' age, sex, educational level, current marital status, medical history, and work status were collected for each patient included in this study. All participants completed test questionnaires which included the 71 items to be tested. These were given to the patients whilst attending the outpatient clinic in addition to brief introduction letter. A trained nurse was available to help when required. The patients' comments and feedback were recorded by the nurse. Nine patients needed help as they forgot their reading glasses or were unable to read the questionnaire. The goal was to obtain a reliable, statistically valid, unidimensional scale that captured as much as possible of: 1. the disability continuum and 2. quality of life affection.

Using Rasch analysis, we used an iterative procedure which balanced 4 concerns:

1. removal of misfitting items,
2. maximising scale length,
3. elimination of items with overlapping difficulties,
4. removal of gaps along the disability-difficulty continuum (20).

Using Rasch analysis, the items that best balanced and met the criteria of item fit, scale length, and were evenly spaced to assess functional impairment were selected for the CASQ-FI questionnaire draft (10 items). Similarly the best items to assess quality of life were selected for the CASQ-QoL questionnaire draft (10 items). Discarded pile of items was also reassessed.

For each question in both developed questionnaires (CASQ-FI and CASQ-QoL) there were 4 choices: without any difficulty (=0), with some difficulty (=1), with much difficulty (=2), unable to do (=3). The score of each questionnaire was the sum of individual item score divided by 10 or the mean of the item score if 8 or 9 items were completed. Neither CASQ-FI nor CASQ-QoL was scored if fewer than 8 items were completed. Total score for each questionnaire ranges from 0–3.

Step III: Validity of the developed questionnaire

After development of the new questionnaire, the instrument was pretested for acceptability and feasibility as a self-administered questionnaire in a random sample of AS patients (total no.=30, 26 men/4 women, mean age 40.1±9.3 years). Questionnaire completion was followed by semi-structured interviews to identify any difficulty with instrument completion. In the QoL questionnaire, either one or 2 items were sometimes not applicable. Those were discussing: the ability to work and relationship with the patient's partner (*e.g.* patients who were not in work or who did not have a current partner). A separate fourth option was added to the question scale under the title "Not Applicable". The 'not applicable' questions were excluded from the scoring system and the total score was divided by only the number of questions that have been answered by patient. One hundred and twenty two consecutively recruited AS patients in the outpatient clinic completed the developed questionnaire. A trained nurse was available for help when required. 8 patients needed help with reading the questionnaire (5 forgot their reading glasses, and 3 need help to read the questionnaire). Patients' age, sex, educational level, current marital status, medical history, work status data were also collected for each patient. Any change of the work status/ability secondary to the disease was recorded.

Construct validity was assessed by correlating the scores for the separate instruments to parameters of disease activity: BASFI, BASDAI and BASG in addition to measure of BASMI items as well as enthesitis score (carried out using the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES); range 0–13 (21)). Disease activity was also assessed using the recently introduced Ankylosing Spondylitis Disease Activity Score (ASDAS) (22) using the equation: 0.121 x total back pain +0.11 x patient's global assessment of disease activity +0.073 x BASDAI question 3 = pain and swelling from peripheral arthritis +0.058 x BASDAI question 6 = duration of morning stiffness +0.579 x natural log of CRP (mg/l) +1.

In addition, each patient completed the HAQS (23) questionnaire as well as Hamilton scales for depression and anxiety.

Work ability: Validity of the questionnaire was further assessed in relation to occupational status. The concept of work ability was defined as the self-perceived ability of a patient to perform his/her job, taking into account the specific work demands, individual health condition, and mental resources (24).

To assess an individual's work ability, a self-administered questionnaire, the Work Ability Index questionnaire (WAI), was used (25). In this study, the first item of this questionnaire was used. This first item is referred to as WAI or self-perceived work ability. The first item of the WAI has previously been used in studies to assess work-ability in patients with musculoskeletal disorders (26). Patients were asked to assign a value between 0 and 10 to their current work ability (0 points very low self-perceived work ability and 10 points best self-perceived work ability ever). Patients reporting an inability to work due to ill health were expected to have scores reflecting poorer health and quality of life. To validate this, the correlation between the patients' reported ability to work/absence from work due to inability to do the job because of the disease, and the disease activity parameters scores was assessed.

Step IV: Reliability

The internal consistency reliability of the instrument is the ratio of the true measure variance to the observed measure variance and is the same as Cronbach's alpha. Reliabilities of ≥0.85 are satisfactory (27, 28). Patients were

asked to complete another copy of the CASQ questionnaire for a second time after 2 weeks to assess test-retest reliability. This method reduces the influence of information recall associated with shorter periods of retest and produces a more robust estimate of instrument reliability. The intra-class correlation coefficient (ICC) was used to measure agreement between test and retest.

Stage V: Responsiveness

Responsiveness has been described as the ability of an instrument to measure clinically important change over time with change at present (29). Sensitivity to change of the CASQ-FI and CASQ-QoL was assessed in 72 patients who were treated with anti-TNF therapy. Patients completed the questionnaire twice in their anti-TNF treatment course; once at 0-time before starting the biologic therapy and at 3 month after commencing the treatment. Changes in the questionnaire scores were compared to changes of other disease activity scores (BAS-FI, BAS-DAI and BAS-G).

Translation of CASQ

The translation of the CASQ into Arabic was done following the proposed guidelines by Guillemin *et al*. (30). Three translators were involved who included two professional translators with medical background and one of the authors (YM). Two different professional translators and another author (SY) carried out the back translation. The translators were instructed that it was important to translate the exact activity listed in the original questionnaire precisely and accurately.

CASQ in comparison to ASQoL

The CASQ (the English format) and the ASQoL (31), were completed simultaneously by 82 ankylosing spondylitis patients (65 males, 17 females, mean age 38.9±7.1 years) who meet the modified New York criteria for AS. All patients completed the CASQ, ASQoL as well as questionnaires to assess for BASFI, BASDAI, and BASG. BASMI measurements were also recorded for every patient. Correlations of both CASQ-QoL and ASQoL to parameters of disease activity (BASFI, BASDAI, BASG and BASMI) were carried out.

Local ethical and methodological protocols for approval of the study were followed. All patients who shared in the study signed an informed consent according to the Declaration of Helsinki.

Statistical analyses

- Rasch analysis

The Rasch computer program Winsteps was used in this work (15, 20). The fit of the data to the model is expressed in 2 ways. First the mean square information-weighted statistic (INFIT) provides information about responses given to items around the same difficulty level as the person's ability. Second, the outlier-sensitive statistic (OUTFIT) refers to items whose difficulty level is remote from the person's ability. Taken together, INFIT and OUTFIT allow one to construct a detailed picture of the working of items within a scale. It is usual to see an INFIT/OUTFIT range of 0.7–1.3 to denote adequate fit of the data to the model (32). However, the magnitude of the fit statistics is affected by sample size and, in the case of un-weighted fit statistic (OUTFIT), by the number of items being summated. To have a consistent Type I error rate of approximately 0.05, a critical value for the upper limit of OUTFIT would be 1.3 with 150 persons, 1.2 with 500 persons and 1.1 with 1000 persons samples (33). A poor item fit statistic can indicate poorly constructed or understood items or, when a scale score is assigned by a professional lack of reliability in assignment. Otherwise, poor fit may indicate problems with uni-dimensionality, that is, the item does not "belong" to the construct or attribute being measured. In the Rasch model of disability, functional ability is considered to lie upon a linear "ruler," similar to an ordinary ruler, where no disability is the anchor at one end and maximum disability is the anchor at the other end. The range of disability is expressed in logits, a completely linear measure. An item (question) difficulty (threshold) represents the position in logits that the item occupies on the linear disability scale. By plotting the item thresholds for each measure, it was possible to determine the width of the construct covered by each measure and the manner in which the thresholds mark that construct. Finally, the floor and ceiling percent was calculated for each item.

-Validation of the questionnaire:

Data were presented as frequency tables for categorical variables and mean, standard deviation and 95% confidence interval for interval variables. Floor percent represent the patient that reported the lowest scale level *i.e*. showing no difficulty in performing such activity. While ceiling is referred to patients reporting maximum difficulty in performing the task prescribed. Spearman correlation was used to test correlation of the score calculated with other parameters. Chi-square was used to test association between 2 categorical variables. Cronbach's alpha was calculated to test reliability and internal consistency of the questionnaire items. All statistical manipulation and analyses were performed using the 11th version of SPSS.

Results

Questionnaire analysis

The CASQ-FI questionnaire: The 10 items of the questionnaire (Appendix) displayed adequate fit to the Rasch model. This is denoted by 2 fit statistics, INFIT and OUTFIT. For the number of cases in this study, INFIT and OUTFIT values within the range 0.7 to 1.3 represent adequate fit to the model (INFIT ranged from 0.82–1.01, OUTFIT range 0.80–1.08). The most difficult task was "lie down/sleep on your back" which had an item threshold of -2.460. At the other end of the spectrum "Go up 2 or more flights of stairs" item threshold was 0.844). Other items held intermediate positions. The differences among items, as regards to their difficulty can also be seen in the percentages of patients selecting each category of a given item.

CASQ-QoL questionnaire: 10 items (Appendix) displayed adequate fit to the Rasch model (INFIT ranged from 0.88–0.99, OUTFIT range 0.80–1.05). The most frequently listed areas affected by AS were: Relation with partner, sleep and worry about the future (item thresholds: -1.84; -1.88, and -2.43 respectively) (Table I).

Appendix: Combined Ankylosing Spondylitis Questionnaire (CASQ)

This questionnaire includes information not available from blood tests, X-rays, or any source other than you. Please try to answer each question, even if you do not think it is related to you at this time. There is no right or wrong answer. Please answer exactly as YOU think or feel. Thank you.

CASQ-FI

1. We are interested in learning how your illness affects your ability to function in daily life.
Please tick (√) the ONE best answer that describes your usual abilities OVER THE PAST WEEK:

Over the LAST WEEK, were you able to:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	Unable TO Do
1. Drink from a glass	....……..	……	…….	..……
2. Dress yourself, including tying shoelaces & putting on socks	…...……	……	…….	.....……
3. Bend down to pick up object off the floor	….……	…….	…….	……
4. Sit for long periods of time *e.g*. working on flat topped table or desk	….……	…….	…….	……
5. Walk outdoors on flat ground including crossing the road	….……	…….	…….	……
6. Go up 2 or more flights of stairs	….……	…….	…….	……
7. Play with / look after children	….……	…….	…….	……
8. Do outside work (such as DIY/ gardening/ lifting)	….……	…….	…….	……
9. Lie down / sleep on your back	….……	…….	…….	……
10. Turn your head whilst reversing your car or use the rear view mirror?	….……	…….	…….	……

CASQ-QoL

This questionnaire helps to assess the holistic impact of the disease and its treatment on your life. Please try to answer each question, even if you do not think it is related to you at this time. There is no right or wrong. Answer. Please tick (√) the one response that best describes what you think or feel. Thank you

Over the LAST WEEKdid you feel able to:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	Unable TO Do	Not Applicable
1. Get a good night's sleep?	….……	…….	…….	……	……
2. Deal with the usual stresses of daily life?	….……	…….	…….	……	……
3. Cope with social/ family activities?	….……	…….	…….	……	……
4. Deal with feelings of anxiety or being nervous?	….……	…….	…….	……	……
5. Deal with feelings of low self-esteem or feeling blue?	….……	…….	…….	……	……
6. Get going in the morning?	….……	…….	…….	……	……
7. Do your work as you used to do?	….……	…….	…….	……	……
8. Deal with any worries about your future?	….……	…….	…….	……	……
9. Continue doing things you used to do, despite tiredness?	….……	…….	…….	……	……
10. Continue your relationship with your partner (husband/wife)?	….……	…….	…….	……	……

Results of validation studies

The main characteristics of the studied sample (no. of patients 122) are demonstrated in Table II. Assessment of flooring and ceiling percentages in the 4 instruments assessed in this study revealed that for HAQ-S: the mean score was 2.2±0.6 whereas the percentage of patients at floor were 16.8% and patients at ceiling were 12.4%; regarding, CASQ-FI: the mean score was 2.3±0.7, percentage of patients at floor was 16.8% and percentage at ceiling was 22.8%; for CASQ-QoL: the mean score was 2.4±0.8, percentage of patients at floor was 16.4% and percentage at ceiling was 20.6%; whereas for ASQoL: the mean score was 17.0±1.2, percentage of patients at floor was 6.2% and percentage at ceiling was 38.9%. Dressing (including tying shoelaces) and lying down in CASQ-FI showed the best correlates with total score, though all items were significantly correlated with total score. Table III shows that there was a significant correlation of BAS-MI with the 4 tools assessed in this study: CASQ-FI, CASQ-QoL, HAQ-S and ASQoL. Cervical rotation ability was significantly associated with better scores of HAQS, CASQ-FI as well as CASQ-QoL ($p<0.001$), whereas ASQoL did not show a significant association with degree of cervical rotation. In comparison to ASQoL and HAQS, both CASQ-FI and CASQ-QoL showed better correlations with BAS-FI, BASDAI and BASG whilst HAQS showed the least r-values though remained significant. Studying the correlation of the new questionnaires for functional disability and quality of life with BAS-FI, BAS-DAI, BAS-G and ASDAS revealed that: r-values for CASQ-FI were 0.85, 0.71, 0.64 and 0.89 respectively ($p<0.001$), and for CASQ-QoL, r-values were 0.86, 0.87, 0.79 and 0.89 respectively ($p<0.001$). In contrast, studying the correlation of ASQoL to the disease activity parameters BAS-FI, BAS-DAI, BAS-G and ASDAS revealed r-values were 0.79, 0.63, 0.60 and 0.81 respectively ($p<0.001$) whereas HAQ-S r-values were 0.38, 0.41, 0.22 and 0.47 respectively (0.01). Variability was minimal in ASQoL (This could be attributed to the small scale responses: Yes/No). ASQoL showed the least values for Cronbach's Alpha (CASQ-FI: 0.96, CASQ-QoL: 0.97, HAQS: 0.86, whereas ASQoL: 0.38). Figure 1 is a scatter plot displaying correlation between BAS-FI and CASQ-FI as well as CASQ-QoL and ASQoL.

All instruments assessed demonstrated a significant correlation ($p<0.001$, r=0.82) with work ability recorded by the patient using the WAI tool. Table IV shows that there was significant correlation ($p<0.001$) of the different levels of work ability reported by the patients with the disease activity parameters,

Table I. Item thresholds of both CASQ-FI and CASQ-QoL questions.

CASQ-FI Questions	Item threshold	CASQ-QoL Questions	Item threshold
Sitting	1.96	Social activities	1.68
Drink from a glass	1.45	Get going in the morning	1.47
Dressing	1.45	Depression	0.98
Bending	1.27	Anxiety	0.86
In and out of the car	1.26	Life stresses	0.47
Going upstairs	0.84	Tiredness	-0.26
Do outside work	-0.97	Work	-1.26
Playing with children	-1.46	Night sleep	-1.84
Driving	-2.27	Relation with partner	-1.88
Lying down	-2.46	Worry about future	-2.43

CASQ-FI: Combined Ankylosing Spondylitis Questionnaire-Functional Disability; CASQ-QoL: Combined Ankylosing Spondylitis Questionnaire-Quality of Life.

Table II. Main characteristics of the studied patients (122 patients, mean age: 38.9±8.7 years, mean disease duration 12.1±4.2 years).

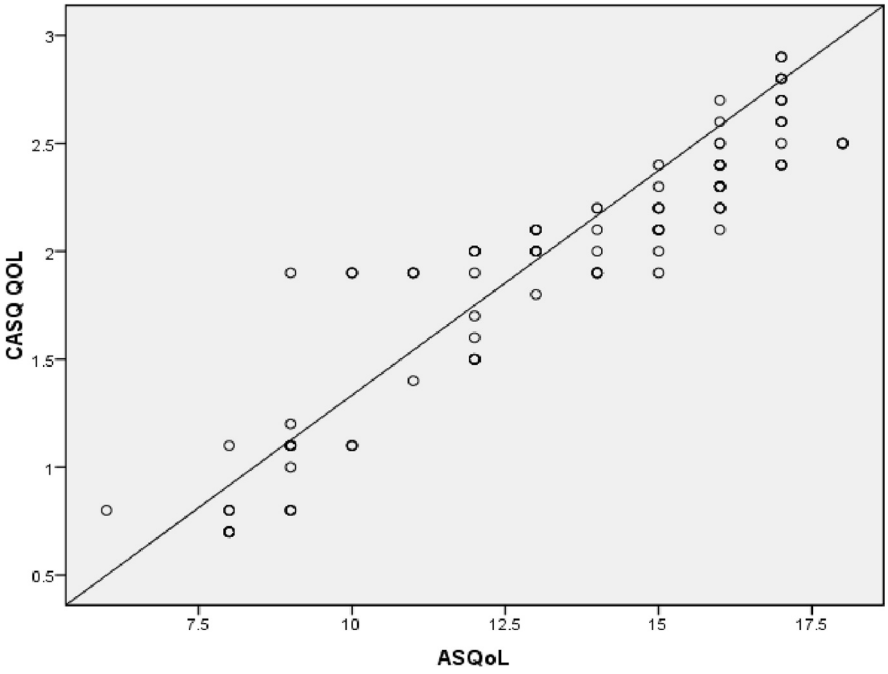
Parameter	Statistic	Parameter	Statistic
BAS-G (0-10)		BAS-FI (0-10)	
Mean (SD)	8.78 (0.7)	Mean (SD)	8.61 (1.7)
95% CI	8.66 – 8.91	95% CI	8.29 – 8.93
BAS-DAI (0-10)		Enthesitis (0-13)	
Mean (SD)	8.54 (0.6)	Mean (SD)	9.16 (2.5)
95% CI	9.43 – 9.66	95% CI	8.69 – 9.63
HAQ-S (0-3)		CASQ-FI (0-3)	
Mean (SD)	2.16 (0.6)	Mean (SD)	2.29 (0.7)
95% CI	2.05 – 2.27	95% CI	2.17 – 2.41
CASQ-QoL (0-3)			
Mean (SD)	2.18 (0.6)	ASDAS	2.73 (0.99)
95% CI	2.07 – 2.28		2.71– 2.75

BAS-DAI: Bath Ankylosing Spondylitis-Disease Activity Index; BAS-FI: Bath Ankylosing Spondylitis-Functional Index; BAS-G: Bath Ankylosing Spondylitis-Global score; HAQ-S: Health Assessment Questionnaire-Spondylitis; ASDAS: Ankylosing Spondylitis-Disease Activity Score; CASQ-FI: Combined Ankylosing Spondylitis Questionnaire-Functional Disability; CASQ-QoL: Combined Ankylosing Spondylitis Questionnaire-Quality of Life.

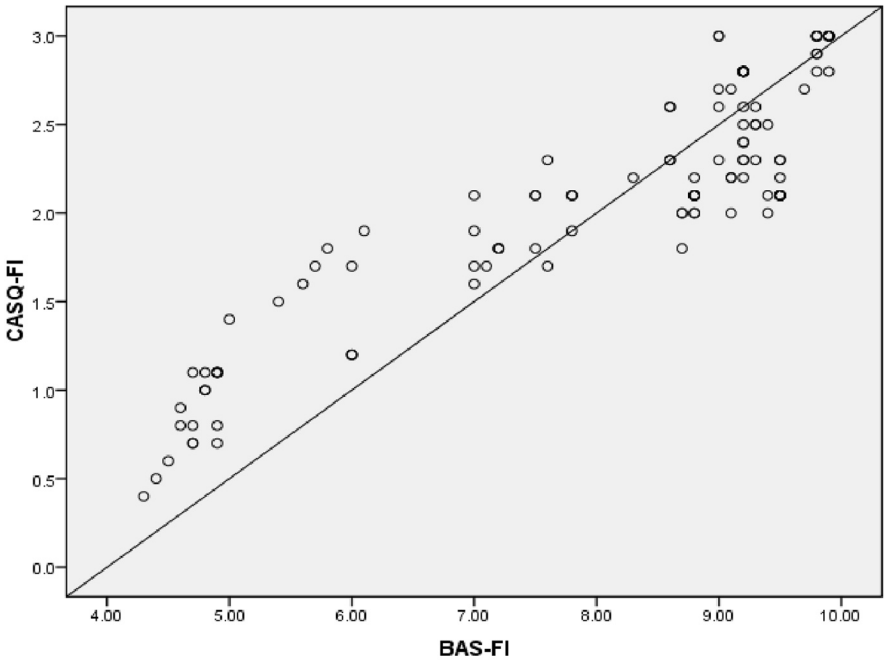
Table III. Correlation of BAS-MI with CASQ-FI, CASQ-QoL, HAQ-S and ASQoL.

	Spearman (r)	*p*-value
CASQ-FI	-0.175	0.01
CASQ-QoL	-0.269	0.004
HAQ-S	-0.112	0.03
ASQoL	-0.244	0.009

CASQ-FI: Combined Ankylosing Spondylitis Questionnaire-Functional Disability; CASQ-QoL: Combined Ankylosing Spondylitis Questionnaire-Quality of Life; HAQ-S: Health Assessment Questionnaire Spondyloarthritis; ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire.



A. Scatterplot displaying correlation of ASQoL score with CASQ-QoL score.



B. Scatterplot displaying correlation of BAS-FI score with CASQ-FI score.

Fig. 1. The correlation between CAS-FI and CASQ-QoL with both BAS-FI and ASQoL parameters.

functional disability and quality of life tools assessed in this study. Work disability was significantly (p<0.001, r=0.86) correlated to disease duration. Compared with those unable to work due to ill health, working patients had significantly better levels of functional ability and quality of life (p<0.001).

Correct completion of the CASQ was assessed. CASQ-FI as well as CASQ-QoL scores were computable for all patients returning the questionnaires.

Reliability

The CASQ was reliable as demonstrated by a relatively high-standardised alpha value (CASQ-FI: 0.96, and CASQ-QoL: 0.97) and minimal changes recorded in the 2nd from the 1st test. ICC for agreement demonstrated a quite good reliability of both CASQ-FI and CASQ-QoL (ICC were 0.96 and 0.96 respectively).

Responsiveness

On studying the correlation of percentage changes in CASQ-FI and CASQ-QoL to percentage changes of parameters of disease activity, a statistically significant correlation was observed between percentage changes of both CASQ-FI and CASQ-QoL on one side and BAS-G, BAS-FI and BAS-DAI on the other side (Table V). The average percentage of change for CASQ-FI was 68.8±31.02 (95% CI 59.9–77.6) whereas for CASQ-QoL percentage of change was 69.3±33.3 (95% CI 59.8–78.7).

Discussion

To provide the most effective management in the care of AS patients, treatment regimens have to be evaluated in terms of their ability both to control the disease and improve quality of life (11). This study represents a comparative evaluation of an evidence-based selection of disease specific, patient–assessed instrument. The CASQ questionnaires have been developed as a tool to assess for functional disability as well as quality of life separately among AS patients. The validation results of this study suggest that the CASQ tool is valid and reliable. Correlations with disease activity parameters were of a sufficient significant magnitude to suggest that the instrument is measuring related aspects of disease specific health. Further evidence for the validity of the instrument was provided by the significant association with work status. A recent study done to assess the psychometric outcome measures in early *versus* late AS patients using the CASQ, revealed that the patients' priorities for outcomes change during the course of the disease. CASQ was a valid tool to identify functional disability as well as quality of life changes in both early and late AS (34).

Most AS patients present with multiple co-existing problems, therefore, a multi-dimensional approach for health state evaluation have been recom-

Table IV. Correlation of the different levels of work ability reported by the patients with the disease activity parameters, functional disability and quality of life tools assessed in this study.

Parameter	Work ability			*p*-value
	Able	Light work	Unable	
BAS-G	7.97 (0.1)	8.79 (0.5)	9.11 (0.7)	<0.001**
BAS-FI	4.90 (0.0)	8.99 (0.9)	9.62 (0.4)	<0.001**
BAS-DAI	8.20 (0.0)	9.72 (0.3)	9.85 (0.2)	<0.001**
CASQ-QoL	1.2 (0.3)	2.18 (0.2)	2.88 (0.3)	<0.001**
HAQS	0.90 (0.1)	2.36 (0.3)	2.41 (0.03)	<0.01*
CASQ-FI	1.10 (0.2)	2.19 (0.3)	2.91 (0.2)	<0.001**
ASQoL	14.70 (0.5)	17.04 (0.7)	17.86 (0.3)	<0.001**

ASDAS: Ankylosing Spondylitis-Disease Activity Score; ASQoL: Ankylosing Spondylitis-Quality of Life; BAS-DAI: Bath Ankylosing Spondylitis-Disease Activity Index; BAS-FI: Bath Ankylosing Spondylitis-Functional Index; BAS-G: Bath Ankylosing Spondylitis-Global score; HAQS: Health Assessment Questionnaire-Spondylitis; CASQ-FI: Combined Ankylosing Spondylitis Questionnaire-Functional Disability; CASQ-QoL: Combined Ankylosing Spondylitis Questionnaire-Quality of Life.

Table V. Correlation of percentage changes of CASQ-FI and CASQ-QoL to percentage changes in other validated instruments.

Parameter	Percentage changes	
	CASQ-FI	CASQ-QoL
BAS-G	0.94**	0.92**
BAS-FI	0.97**	0.95**
BAS-DAI	0.96**	0.95**
ASDAS	0.98**	0.95**

**p<0.0.1

ASDAS: Ankylosing Spondylitis-Disease Activity Score; BAS-DAI: Bath Ankylosing Spondylitis-Disease Activity Index; BAS-FI: Bath Ankylosing Spondylitis-Functional Index; BAS-G: Bath Ankylosing Spondylitis-Global score; HAQS: Health Assessment Questionnaire-Spondylitis; CASQ-FI: Combined Ankylosing Spondylitis Questionnaire-Functional Disability; CASQ-QoL: Combined Ankylosing Spondylitis Questionnaire-Quality of Life.

mended (35). The activity limitation concept has been defined as the capacity to perform the usual daily activities for a person's age and major social role (36). Quality of life has been clearly differentiated from activity limitation. Quality of life goes beyond impairment and activity limitation by asking what the patient's health prevents them from doing and also about their emotional response to these restrictions (6, 37). Furthermore, quality of life illustrates the patient's perception about his role in life in general. The developed CASQ addressed these 2 main domains of disease impact: functional impairment and quality of life aiming at assessing them in one step with a simple, validated and reliable tool.

Instrument selections must consider available evidence in light of the proposed application. Although many developers involve patients in item generation to ensure the representation of patient concerns, patient-assessed instruments typically use summated rating scales that use standardised items. By providing the opportunity for identification of areas of life that a patient deems to be of greatest importance, the CASQ allowed an individual perspective to be considered within the evaluation process. Similar approach was used in another study carried out by Haywood *et al*. who developed a Patient Generated Index using a patient centred approach to assess AS-specific health related quality of life (38). Results of the Rasch analysis model reported in this study agree with earlier findings reported by Eyres *et al*. (39) and Haywood *et al*. (38). Rasch analysis provided statistical methods to identify items that do not "fit" the hypothesized uni-dimensional model or that are not answered accurately.

The 10 questions included in the CASQ-FI covers the main disability items among patients with AS and would therefore space out the individual difficulties as evenly as possible. Each question, moreover, has sublevels of difficulty, and each level represents a separate measure of difficulty. Thus, the 10-item CASQ-FI questionnaire can represent 3x10 separate levels of difficulty or 30 item thresholds. Results of this study revealed that the 10-item scale is easier than the HAQS to use and score in the clinic and in research studies. In contrast, the HAQS questionnaire which was developed primarily for rheumatoid arthritis, and as such, has been amended to assess disability among patients with AS. However, the characteristic impairment to the axial skeleton found in AS produces a different range of disabilities and functional problems. Consequently, the HAQS is of limited value for use among AS patients, despite the inclusion of five additional items specific to the disease (17). The validation studies of the CASQ-FI show that it was sensitive to change after commencing anti-TNF therapy. In addition, it is strongly related to clinical and outcome variables as in the HAQS or even more.

Matching the WHO-International classification of functioning, disability and health (ICF) recommendations regarding the integration of functional disability, psychological status and society interaction in the clinical assessment of chronic diseases (4), the developed CASQ offered this mix in 2 separate domains. Other health related measures used in AS included SF-36, Dougados Functional index (DFI) and the Leeds Disability Questionnaire. Davis and colleagues chose the SF-36 to assess changes in health status in patients with AS treated with etanercept (40). For a US cohort consisting of 40 patients, significant improvements in score were found after 16 weeks on 5 of the eight domains. Furthermore, Turan *et al*. reported that AS ill-health is not related to social functioning or mental health as assessed by the SF-36 (41). Given that SF-36 is not specific to AS and has relatively poor psychological properties it is difficult to justify its use for AS

patients. The DFI, a single item scale, is widely used and contains 20 items covering activities of daily living. It has been criticised for providing a limited reflection of core assessment domains, lacking sensitivity and for omitting key activities that present difficulties for AS patients (17, 42). The revised Leeds disability questionnaire has not been recommended for application due to poor data quality; the limited range of functional disability assessed and limited responsiveness (43).

Currently one AS-specific measure of QoL is commonly used, the ASQoL (30). In general quality of life measures, should adopt the needs-based model. This model states that individuals are driven or motivated by their needs and that life derives its quality from the ability and capacity of the individual to satisfy certain human needs (44). However, though the ASQoL purports to measure AS-related quality of life, it does not include some of the most important and frequently mentioned patients concerns (12). This would explain the discrepancy of the correlation levels of the CASQ-QoL *versus* ASQoL when assessed against BASMI measures (Table IV). Moreover, the ASQoL has a dichotomous response scale which often fails to support sufficiently detailed descriptions of health (39, 45, 46). In addition, there is an overlap between ASQoL and BASDAI items. In comparison to the ASQoL, the CASQ-QoL also covered items such as working outside the home and relationship with the partner.

Reliability remains an important issue when selecting instruments for individual evaluation (47). Results of this study showed that the CASQ-FI demonstrated good level of reliability that is comparable to HAQS. Similarly, in comparison to the published ASQoL data (31), the CASQ-QoL had higher Cronbach's α value (Cronbach's alpha was 0.966 for CASQ-QoL, whereas in ASQoL it ranged between 0.87–0.91). In the test-retest reliability the ICC for CASQ-QoL was 0.956, whereas for ASQoL it ranged between 0.91–0.92. In addition, CASQ-QoL showed higher correlation estimates (r-value) with BASFI, BASDAI, BASG as well as other clinical validating tools used. Boonen *et al*. (48) investigated the use of European quality of life (Euro-QoL) and Short Form-6D (SF-6D) among AS patients in an attempt to decide which was more useful for clinical studies. Both scales had very low levels of test/retest reliability (Euro-QoL=0.55, SF-6D=0.68). Such levels imply high levels of measurement error (up to 70%); consequently little confidence could be placed on the scores obtained by patients on these measures. In that study, the BASDAI and ASQoL were also used to evaluate the impact of active spa treatment for AS. Both measures were able to show marked improvement in score following 3 weeks of treatment.

Assessment of the evidence of measurement properties following completion of the CASQ revealed that it has a good completion rate, in comparison to HAQ and HAQ-S questionnaires which have poor data quality. The ASQoL has good completion rates, satisfactory data quality, and some evidence of validity.

Ankylosing spondylitis is associated with a relatively early age at onset, making the impact of pain, fatigue, and progressive disability on the patient's career and workability are likely to be long-term and far-reaching (49). Results of this study revealed that work disability correlated significantly with disease duration. An earlier study revealed that up to 36% AS patients may have their working ability affected primarily depending on disease duration (7). The correlation to disease duration is important to notice since AS evolves slowly and progressively mainly in patients in their 3rd decade. Allaire (50), reported that work disability among AS patients is a multidimensional construct encompassing not only employment per se but also reduced working hours, loss of promotional opportunities, increased use of sick leave, frequent job changes, and early retirement. Given its importance, it is plausible to incorporate assessment of work ability in AS patients in their standard clinical management.

In conclusion, The CASQ was found to be a valuable tool that is reliable and valid for assessment of functional impairment and quality of life in AS. The CASQ is well accepted by patients, sensitive to change, easy to administer and score in AS patients. The developed CASQ can be used in many places where other tools to assess functional disability and quality of life are now used. The CASQ-FI and CASQ-QoL questionnaires can be used and scored separately, to assess for functional disability as well as quality of life respectively, or in combination to assess for both parameters individually.

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