Longitudinal validation of King's Sarcoidosis Questionnaire in a prospective cohort with mild sarcoidosis

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Shareable abstract (@ERSpublications)
This study advances the validation of King's Sarcoidosis Questionnaire by known-groups validity and assessments of responsiveness, demonstrating good reliability, validity and responsiveness for assessing quality of life in a cohort with mild sarcoidosis https://bit.ly/3UYrcSn

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Abstract

Background Quality of life is impaired in patients with sarcoidosis. The King's Sarcoidosis Questionnaire (KSQ) is a brief questionnaire assessing health-related quality of life in patients with sarcoidosis, comprising subdomains of General Health Status (GHS), Lung, Medication, Skin and Eyes. The aim of this study was to enhance the validation of the KSQ, incorporating longitudinal validation and known-groups validity in a cohort with mild sarcoidosis.

Methods The KSQ was linguistically validated according to guidelines. Patients with sarcoidosis completed KSQ and other questionnaires at baseline, after 2 weeks and at 12 months. Forced vital capacity (FVC) was measured. Concurrent validity, reliability and responsiveness were assessed.

Results In patients (n=150), the KSQ had moderate to strong correlations with the Short Form-12 (Mental Component Summary), the King's Brief Interstitial Lung Disease questionnaire and the Fatigue Assessment Scale (r=0.30–0.70) and weak correlations with the Short Form-12 (Physical Component Summary) and FVC (r=0.01–0.29). The KSQ GHS and Lung domains were able to discriminate between groups of patients stratified according to fatigue, treatment and FVC. The KSQ had high internal consistency (Cronbach's α=0.73–0.90) and repeatability (interclass correlation coefficients 0.72–0.81). Correlations to comparable questionnaires at baseline were moderate or strong for the GHS, Lung and GHS–Lung subdomains and weak or moderate for FVC. The KSQ was responsive to changes over time.

Conclusion This study strengthened the validation of the KSQ by introducing known-groups validity and assessments of responsiveness over 12 months in patients with mild sarcoidosis.

Introduction

Sarcoidosis is a highly variable granulomatous disease of unknown aetiology. Sarcoidosis primarily involves lungs and intrathoracic lymph nodes, but can potentially affect any organ. Many patients have mild and self-limiting disease; some have a more chronic trajectory, and a minor subset of patients develop severe sarcoidosis with permanent organ dysfunction.

Disease extent and activity are determined from objective measures such as pulmonary function tests, blood assays and imaging. It is increasingly recognised that many patients with sarcoidosis have impaired health-related quality of life (HRQoL) and a great burden of symptoms often not correlated to parameters of disease activity [1, 2]. Patient-related outcome measures (PROMs) have not routinely been included in the follow-up of patients with sarcoidosis. In a survey, patients with sarcoidosis rated their quality of life and functionality as the most important outcomes in management of the disease [3]. Quality of life has been recommended as an end-point in clinical trials [4]. This emphasises the importance of including PROMs in the overall assessment of sarcoidosis severity and impact on patients' lives, and the need for clinically applicable and validated questionnaires.

Different PROMS have been used in sarcoidosis, although few are disease-specific [5]. The King's Sarcoidosis Questionnaire (KSQ) is a brief questionnaire assessing HRQoL in patients with sarcoidosis. The KSQ was developed and validated in an English sarcoidosis cohort [6] and has been validated in other languages [7, 8], but further validation is needed. To our knowledge, the 12-month longitudinal performance of the KSQ has not previously been assessed, nor has the KSQ been validated in sarcoidosis patients with milder disease.

This study aimed to validate the KSQ, including longitudinal validation over a 12-month period and known-groups validity, in a population with mild sarcoidosis. Mild sarcoidosis was defined as patients with mean preserved pulmonary function; the majority had Scadding stage 0 or I and, compared with previous studies, there was a smaller subset of patients with extrapulmonary organ involvement, need for treatment and long disease duration [6, 8–10].

Methods

Study population

The study was a prospective observational cohort study. From December 2019 to December 2021, patients with sarcoidosis were consecutively recruited from the Center for Rare Lung Diseases, Aarhus University Hospital, Denmark. Adult patients with a diagnosis of sarcoidosis based on the most recent American Thoracic Society diagnostic criteria [9] and who were able to understand and complete the questionnaires were eligible for inclusion. The sample size arrived from these criteria. Participants provided written informed consent.

The study was approved by the Central Denmark Region Data Protection Agency (case number: 1-16-02-90-19) and acknowledged by the Central Denmark Region Committee on Health Research Ethics.

Questionnaires

The KSQ is a 29-item questionnaire with five domains: General Health Status (GHS) (10 items), Lung (six items), Medication (three items), Skin (three items) and Eyes (seven items), scored on a seven-point Likert scale. The GHS domain is administered to all patients and additional domains are completed individually depending on organ involvement and treatment. The total health status score is determined by combining the modules (*e.g.* GHS–Lung). Scoring is calculated using a re-ordered scale for appropriate items; higher scores indicate better HRQoL [6]. The minimal clinically important differences (MCIDs) have been estimated for the KSQ GHS and Lung modules: 8 for GHS and 4 for Lung [10].

Linguistic validation

The KSQ was translated into Danish following acknowledged guidelines [11]. Initially, a forward translation was performed by two translators whose first language is Danish. The two versions were merged, and consensus was reached on any differences between the two translations. A translator whose first language is English, blinded to the original English version, back-translated the merged version, and the original author reviewed the translation.

10 patients with sarcoidosis of different gender, age, radiologic stage and organ involvement completed the questionnaire followed by a semi-structured interview. Patient interviews were subsequently reviewed by an expert panel.

The King's Brief Interstitial Lung Disease (K-BILD) is a 15-item questionnaire used for HRQoL measurement in different interstitial lung diseases. This questionnaire was included, as many sarcoid patients exhibit interstitial lung changes. Patients score on a seven-point Likert scale, resulting in a total score (Tot) and three domain scores: psychological (Psy), breathlessness and activities (BA) and chest symptoms (CS). Scores range from 0 to 100; higher scores indicate better HRQoL. K-BILD was validated in a large Danish cohort of patients with idiopathic pulmonary fibrosis [12, 13].

The Short Form-12 (SF-12) is a 12-item generic outcome measure assessing the impact of health on everyday life in a three- to five-point Likert scale. The SF-12 is a shortened version of the Short Form-36 (SF-36), created to reduce the burden of response. Scores are recorded on eight health domain subscales, and a weighted sum of these scores is converted to a T-score (mean 50, standard deviation 10); lower T-scores indicate worse HRQoL. Results are gathered in a Physical Component Summary (PCS) and a Mental Component Summary (MCS) used for the criterion-based interpretation [14].

The Medical Research Council (MRC) Dyspnoea Scale is a one-item, 5-point score grading of the effect of breathlessness on daily activities, with a high score indicating severe dyspnoea.

The Fatigue Assessment Scale (FAS) is a 10-item questionnaire designed to assess fatigue in the general population and subsequently validated in a sarcoidosis setting [15]. The five response categories range from "never" to "always" and the total score ranges from 10 to 50, with higher scores indicating more fatigue.

The Global Rating of Change Scale (GRCS) is a single-item, 11-point instrument assessing the perception of improvement/deterioration over time [16].

All questionnaires were self-reported.

Study procedure

At inclusion, patients completed the KSQ, the SF-12, the K-BILD, the MRC Dyspnoea Scale and the FAS; after 14 days, the KSQ and the GRCS were completed. After 12 months, the KSQ, the SF-12, the K-BILD, the MRC Dyspnoea Scale and the FAS were completed.

Data on demographics, organ manifestations, pulmonary function tests, Scadding stage and treatment were retrieved from medical charts. Patients self-completed the questionnaires when attending the clinic after medical consultation. After 14 days, the KSQ and the GRCS were completed at home. Questionnaires with <85% completion were excluded.

Psychometric validation and statistical analysis

Reliability

- Internal consistency, the inter-relatedness of the items in the questionnaire, was estimated by calculating Cronbach's α for each domain. Values >0.7 indicate a sufficient level of internal consistency [17].
- Test–retest reliability was evaluated by intraclass correlation coefficients (ICCs) and Bland–Altman plots comparing the KSQ scores at baseline with those at 14 days in stable patients. Patients with a score of −1–1 in the GRCS at 14 days were considered stable. ICC values >0.7 are considered reliable measures of reliability [18]. The limits of agreement were calculated as mean±1.96×$_{SD}$ of within-subject differences.

Validity

Concurrent validity was assessed by measuring the correlation of the KSQ to the SF-12, the K-BILD, the MRC Dyspnoea Scale, the FAS and forced vital capacity (FVC) using the Pearson correlation coefficient. A correlation coefficient of <0.30 is considered weak, 0.30–0.50 moderate, and >0.50 strong.

Normal distribution of data was assessed using histograms and Q–Q plots. Categorical variables are presented as percentages of the total population. The t-test was used to evaluate differences among genders. Variance homogeneity was assessed using the F-test. For non-normal data, the Spearman correlation was applied.

Known-groups validity was investigated by estimating the ability of the KSQ to distinguish between groups of patients with different severity of disease. Patients were stratified into "known groups" according to their fatigue score, FVC and need for treatment. The independent two-sample t-test was used for comparison when scores in the known groups followed a normal distribution; otherwise, the Wilcoxon–Mann–Whitney test was applied. Effect sizes were calculated from ANOVA and were reported as partial η^2: small effect 0.01, medium effect 0.06 and large effect 0.14.

Responsiveness

The ability to detect changes over time was assessed by measuring changes in the KSQ over 12 months and correlating those to changes in the SF-12, the K-BILD, the MRC Dyspnoea Scale, the FAS and FVC using the Pearson correlation coefficient. Non-normal data were logarithmically transformed; otherwise, the Spearman correlation was applied. Weaker correlations than concurrent validity were expected due to larger variations in changes in the two measures.

Analysis

Analyses were conducted using the Stata/BE 17.0 for Mac statistical software package.

We hypothesised good correlations of the GHS to the SF-12 and the FAS and a good correlation between the Lung subdomain and the K-BILD and the MRC Dyspnoea Scale. We expected a poorer correlation of the KSQ to FVC.

We expected negative correlations for the MRC Dyspnoea Scale and the FAS due to inverse scoring scales.

Missing data, lost to follow-up, withdrawal of consent, death and other similar developments were managed by data reduction.

Results

Linguistic validation

No major issues were identified during the translation process. Minor differences between the two translations were resolved by review and discussion. The back-translation was approved by the original author. Patient interviews demonstrated high face and content validity of the Danish version of the KSQ (see supplementary material). Evaluation of patient interviews in the expert group did not necessitate any further adaptations.

Participants

A total of 163 patients met the inclusion criteria. Of these, 150 patients accepted participation and completed the KSQ at baseline. The demographics of patients are shown in table 1. After 12 months, 128 patients completed the KSQ. Of the remaining, two had died, four were lost to follow up, six withdrew their consent and 10 did not complete or were not provided the questionnaire.

Most participants were male, and the cohort was relatively mildly affected, as judged from pulmonary function tests, Scadding stage, number of patients with extrapulmonary organ involvement and need for treatment. The majority (63%) were incident patients who had been diagnosed within the preceding 6 months; the rest had been diagnosed in the preceding 3 years. Extensive baseline characteristics of the cohort have been described previously [2]. The KSQ-GHS score was significantly higher in men (mean 68, 95% CI 64.5–70.7) than in women (mean 61, 95% CI 56.6–64.7) (mean difference −7, 95% CI −12.0–−2.0). Patients with fatigue (FAS score ⩾22) had a significantly worse GHS score (55.2, 95% CI 52.5–57.3) than patients with lower fatigue scores (75.7, 95% CI 72.8–78.6) (mean difference 20.8, 95% CI 17.0–24.5).

TABLE 1 Patient demographics at inclusion

Patients, n	150
Age, years, mean (95% CI)	47.4 (45.1–49.8)
Male gender	89 (59%)
Ethnicity, Caucasian	100%
Smoking history	
Never smokers	97 (65%)
Former smokers	42 (28%)
Current smokers	8 (5%)
No answer	3 (2%)
Time since diagnosis, days, mean (95% CI)	300 (245–354)
FEV_1 % of predicted, mean (95% CI)	92 (89–94)
FVC % of predicted, mean (95% CI)	101 (97–103)
D_{LCO} % of predicted[#], mean (95% CI)	84 (81–87)
Scadding stage, chest radiograph[¶]	
0	29 (20%)
I	74 (51%)
II	32 (22%)
III	7 (5%)
IV	3 (2%)
Number of patients with extrapulmonary involvement who completed the KSQ	
Eyes	19 (13%)
Skin	14 (9%)
Treatment	
Glucocorticoids	47 (31%)
Duration of glucocorticoids, days, mean (95% CI)	196 (106–285)
Methotrexate	4 (3%)

Data are presented as n (%) unless otherwise stated. FEV_1: forced expiratory volume in 1 s; FVC: functional vital capacity; D_{LCO}: diffusing capacity of the lung for carbon monoxide; KSQ: King's Sarcoidosis Questionnaire. [#]: n=127; [¶]: n=145.

Psychometric validation

Reliability

All domains of the KSQ showed good internal consistency with Cronbach's α>0.70 (table 2).

Due to the low number of patients with skin and eye involvement, and even lower numbers of completed 14-day follow-up questionnaires, these two subdomains were excluded from further analyses.

Most patients were categorised as stable from their completion of the GRCS after 14 days (table 3). In stable patients, test retest showed high intercorrelation coefficients (>0.7), and thus suggested good reliability of the KSQ (table 3).

Bland–Altman plots for the GHS and Lung domains visualise the agreement between scores at baseline and after 14 days, although both plots contain some outliers outside the 95% limits of agreement. The plot for the Lung domain shows a slight tendency to increased variation with higher scores (figure 1).

Concurrent validity

The GHS domain correlated strongly to the SF-12, the K-BILD and the FAS (with a correlation coefficient range of −0.78 to 0.74), and moderately to the MRC Dyspnoea Scale and FVC (−0.45 to 0.31). The KSQ Lung showed moderate correlations to the SF-12 and FVC and strong correlations to the K-BILD, the MRC Dyspnoea Scale and the FAS.

The GHS–Lung combined correlated strongly (−054 to 0.82) to all tested parameters except FVC (0.38).

The medication domain correlated strongly to the FAS, the K-BILD (Tot and Psy) and the SF-12 (MCS); moderately to the K-BILD (BA and Chest) and the MRC Dyspnoea Scale; and weakly to the SF-12 (PCS) and FVC (table 4).

Known-groups validity

At baseline, patients in the upper quartiles of FVC % predicted (n=35 (18 males), mean age 51.9 years, 95% CI 46.5–57.4) and lower quartiles of the FAS scores (n=37 (27 males), mean age 51.8, 95% CI 47.2–56.4) had significantly higher GHS, Lung and GHS–Lung scores than patients in the lower quartiles of FVC % predicted (n=39 (25 males); mean age 49.3, 95% CI 44.2–54.3) and the upper quartiles of the FAS scores (n=35 (16 males); mean age 44.7, 95% CI 40.0–49.5) (table 5). Patients on or initiating treatment at baseline (n=47 (27 males); mean age 46.5, 95% CI 42.2–50.8) scored significantly lower on total scores than patients without treatment (n=103 (62 males); mean age 48.4, 95% CI 45.7–51.2), visualised for the GHS–Lung (figure 2).

Responsiveness

Over 12 months, the mean HRQoL (GHS and Lung scores) improved significantly (n=128): GHS: 64.66 to 69.57, mean difference 4.91 (95% CI 2.62–7.20); Lung: 66.99 to 70.19, mean difference 3.19 (95% CI 0.23–6.16); GHS–Lung: 67.30 to 70.52, mean difference 3.22 (95% CI 1.50–4.94). Medication scores were stable (n=21): 62.10 to 64.00, mean difference 1.91 (95% CI −13.00–0.17).

Using the MCID of 8 for GHS scores, 60 patients (47%) improved, 21 (16%) deteriorated and 47 (37%) were stable. Using the MCID of 4 for Lung scores, 65 (51%) improved, 39 (30%) deteriorated and 24 (19%) remained stable. There was no difference in the change in KSQ score between treated and untreated patients: GHS, mean difference −0.16 (95% CI 5.43–5.11); Lung, mean difference −2.45 (95% CI −9.24–4.3); GHS–Lung: mean difference: 0.15 (95% CI −3.79–4.10).

TABLE 2 Internal consistency: data represent Cronbach's α for different King's Sarcoidosis Questionnaire (KSQ) domains

KSQ domain	Cronbach's α
General health status (n=150)	0.90
Lung (n=150)	0.85
Medication (n=35)	0.75
Skin (n=14)	0.73
Eyes (n=19)	0.90

TABLE 3 Repeatability of King's Sarcoidosis Questionnaire (KSQ) domains at baseline and after 14 days in stable patients

KSQ domain	n/N (%)	ICC
General health status	88/110 (80%)	0.81
Lung	98/111 (88%)	0.72
Medication	19/22 (86%)	0.75

Data are presented as number of stable patients in (% of responders to Global Rating of Change Scale and KSQ after 14 days). ICC: intraclass correlation coefficient.

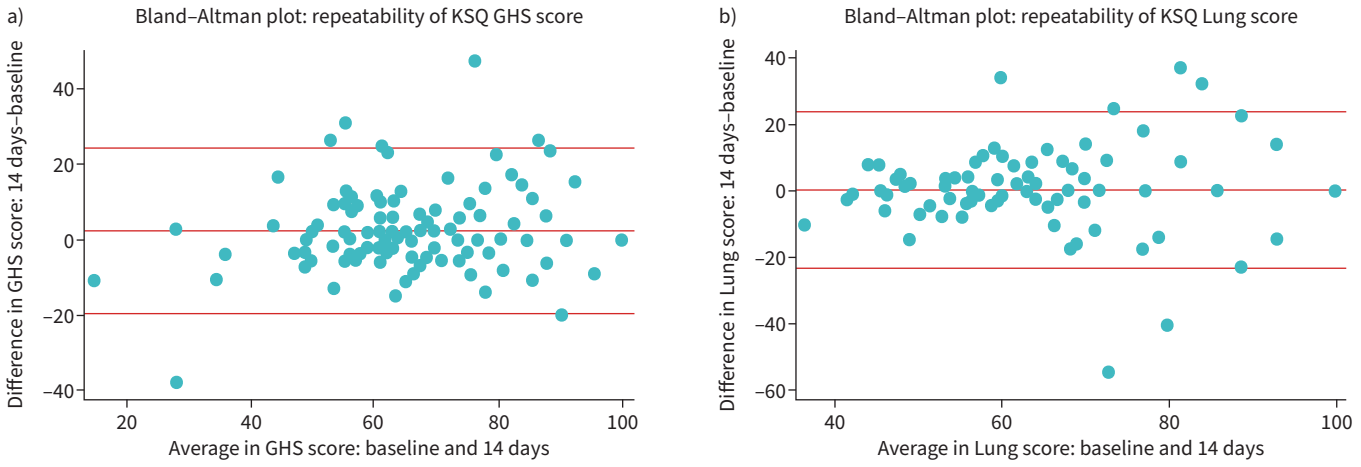

FIGURE 1 Repeatability of King's Sarcoidosis Questionnaire (KSQ): a) General Health Status (GHS) and b) Lung scores.

TABLE 4 Correlations at baseline between King's Sarcoidosis Questionnaire (KSQ) domains and anchors

	SF-12 domain		K-BILD domain						
KSQ domain	**MCS (n=148)**	**PCS (n=148)**	**Tot (n=146)**	**Psy (n=147)**	**BA (n=147)**	**CS (n=148)**	**MRC Dyspnoea Scale (n=146)**	**FAS (n=147)**	**FVC (n=149)**
GHS (n=150)	0.72	0.58	0.74	0.65	0.69	0.55	−0.45	−0.78	0.31
Lung (n=150)	0.48	0.47	0.76	0.55	0.74	0.73	−0.53	−0.52	0.38
GHS–Lung (n=150)	0.67	0.57	0.82	0.66	0.77	0.70	−0.54	−0.54	0.38
Medication (n=35)	0.56	0.25	0.55	0.64	0.39	0.33	−0.35	−0.52	0.29

SF-12: Short Form-12; MCS: Mental Component Summary; PCS: Physical Component Summary; K-BILD: King's Brief Interstitial Lung Disease; Tot: total; Psy: psychological; BA: breathlessness and activities; CS: chest symptoms; MRC: Medical Research Council; FAS: Fatigue Assessment Scale; FVC: forced vital capacity; GHS: General Health Status.

TABLE 5 General Health Status (GHS), Lung and GHS–Lung scores at baseline for the lower (lq) and upper quartiles (uq) of functional vital capacity (FVC) % of predicted, the lq and uq of Fatigue Assessment Scale (FAS) score and for untreated and treated patients

	FVC lq	FVC uq	Mean difference (95% CI)	FAS lq	FAS uq	Mean difference (95% CI)	No treatment	Treatment	Mean difference (95% CI)
GHS	60.6	70.6	9.9 (2.07–17.8)	81.1	49.5	31.7 (26.4–36.9)	67.9	58.0	9.9 (4.7–15.0)
Lung	58.6	74.2	15.6 (9.19–22.1)	77.6	55.8	21.8 (15.3–28.4)	68.2	61.8	6.4 (1.0–11.8)
GHS–Lung	62.8	72.5	9.4 (4.6–14.8)	77.8	57.2	20.6 (16.7–24.5)	69.0	62.8	6.2 (2.6–9.8)

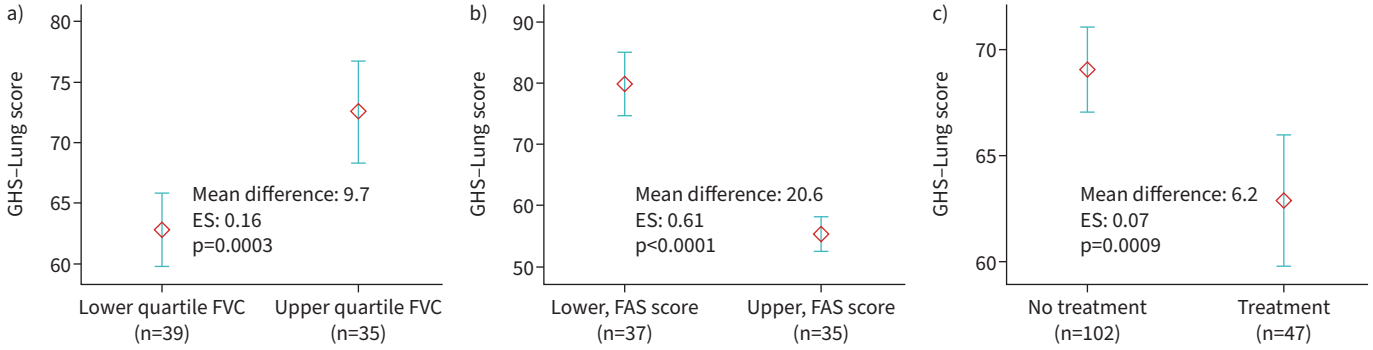

FIGURE 2 General Health Status–Lung (GHS–Lung) score at baseline in: a) the lower and upper quartiles of forced vital capacity (FVC) % of predicted, b) the lower and upper quartiles of the Fatigue Assessment Scale (FAS) score and c) untreated and treated patients. The dots indicate the median; the lines 95% confidence intervals. ES: effect size (partial η^2).

Table 6 shows correlations between changes in the KSQ and changes in anchors from baseline to 12 months.

The correlation of changes in all domains of the KSQ was moderate or strong for the MCS, the K-BILD and the FAS (r=0.30–0.70) and weak for the PCS and FVC (r=0.01–0.29), except for the Medication module correlation to the SF-12.

Discussion

Our study contributes to the validity of the KSQ. To our knowledge, this is the first study to assess 12-month responsiveness, to assess known-groups validity and to investigate the performance of the KSQ in a population with mild sarcoidosis.

We were able to fully validate the GHS, Lung and Medication domains. The KSQ showed good face and content validity.

The KSQ demonstrated high discriminative ability in known groups of patients regarding the FAS score, FVC and treatment. This is supported by the moderate to large effect sizes. Over the 12 months, mean HRQoL improved for the KSQ domains. This is compatible with the overall perception of mild sarcoidosis being a benign disease that tends to naturally resolve within a few years for most patients. This is also in line with the fact that our cohort had mild disease and comprised predominantly incident patients, with a considerable proportion having Löfgren syndrome [2]. The longitudinal validation showed that the KSQ was responsive to change over time and correlated with the anchors at 12 months to a similar degree as it did at baseline. Most correlations were moderate, but due to measurement error on two measures, correlations between changes in scores are expected to be smaller than of the exact values. Baughman *et al.* [10] estimated the MCID for the KSQ (GHS and Lung). They evaluated changes in scores over 6 months in a more severely ill sarcoidosis population and found the strongest correlations with St George's Respiratory Questionnaire, the SF-36 and the FAS, although correlations overall were weaker than in this study.

TABLE 6 Correlations in change (Δ) from baseline to 12 months

	SF-12 domains		K-BILD domains						
KSQ domain	ΔMCS (n=125)	ΔPCS (n=125)	ΔTot (n=125)	ΔPsy (n=125)	ΔBA (n=126)	ΔCS (n=127)	ΔMRC Dyspnoea Scale (n=124)	ΔFAS (n=124)	ΔFVC (n=128)
ΔGHS (n=128)	0.54	0.23	0.54	0.48	0.51	0.42	−0.21	−0.59	0.09
ΔLung (n=128)	0.48	0.24	0.63	0.47	0.70	0.65	−0.30	−0.53	0.19
ΔGHS–Lung (n=128)	0.53	0.29	0.67	0.55	0.66	0.60	−0.31	−0.61	0.18
ΔMedication (n=21)	0.29	0.32	0.45	0.47	0.35	0.51	−0.41	−0.36	0.01

KSQ: King's Sarcoidosis Questionnaire; SF-12: Short Form-12; MCS: Mental Component Summary; PCS: Physical Component Summary; K-BILD: King's Brief Interstitial Lung Disease; Tot: total; Psy: psychological; BA: breathlessness and activities; CS: chest symptoms; MRC: Medical Research Council; FAS: Fatigue Assessment Scale; FVC: forced vital capacity; GHS: General Health Status.

The internal consistency was high, with Cronbach's α>0.70 for all domains. This is comparable to the findings of previous validation studies [6–8].

The KSQ showed good repeatability in terms of test–retest results, with ICC >0.70, which is comparable to the KSQ validation in a Dutch study population [7], although not as high as found in the original study [6]. Repeatability was not tested in the German validation study [8]. However, an increased variability was observed in higher scores for the Lung domain and may be attributed to more similar answer options within the high score range, leading to more inconsistency in patient responses. Alternatively, patients experiencing fewer symptoms may exhibit greater variability over a short period.

The concurrent validity of the questionnaire was high; in particular, we found a strong correlation between the GHS, the Lung and the GHS–Lung domains and the K-BILD total and the FAS.

Contrary to our hypothesis, we found a weak correlation of the KSQ domains to the SF-12 (PCS), compared with studies using the SF-36 and the World Health Organization Quality of Life (WHOQOL), indicating that the SF-12 is a less reliable generic questionnaire for sarcoidosis. The better correlation of the KSQ to the SF-12 (MCS) than the correlation to SF-12 (PCS) probably reflects that health status and quality of life in patients with sarcoidosis are greatly influenced by fatigue and mental/psychological factors. This tendency was also observed in the original British and German studies when correlating to the SF-36 (PCS and MCS) [6, 8].

We chose the K-BILD as an anchor because it is short, easy to complete and validated in interstitial lung disease, compared with, for instance, St George's Respiratory Questionnaire, which is longer, is more complicated and was developed for COPD. We considered sarcoidosis to have more similarities to interstitial lung disease than to COPD in general, which is supported by our results showing a good correlation between the KSQ and the K-BILD.

As hypothesised, the correlations of the KSQ domains with FVC were poor, although best for the Lung domain. This has been noted several times before [6, 7, 10]. Fatigue has a huge impact on quality of life in patients with sarcoidosis [19], and the poor correlations of fatigue to clinically relevant measures have previously been demonstrated in Danish sarcoidosis patients and in other cohorts [2, 20, 21]. Furthermore, the moderate to high correlation of all the KSQ domains to the FAS suggests that the KSQ captures the influence of fatigue on quality of life.

The worse HRQoL in women was compatible with findings in the original study and, although not significant, the Dutch study [6, 7]. This may be explained by the fact that women report more fatigue than males in this and other cohorts [2, 22, 23].

The Medication module correlated better to anchors than in the previous studies [6, 8]. It had high correlation to the SF-12 (MCS), the K-BILD (Tot and Psy) and the FAS. Side effects of mainly steroid treatment may contribute to Medication scores.

Overall, the baseline validation of the KSQ showed that it is also valid, reliable and able to distinguish between groups of sarcoidosis patients with different stages of disease in a population with mild sarcoidosis, thus increasing the applicability of the KSQ across a wider spectrum of sarcoidosis patients.

In terms of generalisability to the broader population of sarcoidosis patients in Denmark, our cohort exhibited an age and gender distribution remarkably similar to the most recent population-based register study [24]. This study indicated that 45.6% of patients were prescribed treatment within 3 months to 3 years after diagnosis, a figure slightly higher than that observed in our present study, albeit over a longer time frame. Currently, there is a scarcity of recent clinical data on sarcoidosis in Denmark. However, Viskum and Thygesen's report on spirometry data from a Danish sarcoidosis cohort spanning from 1954 to 1970 sheds some light on the matter. Their findings revealed that 20% of the patients had abnormal spirometry results, mirroring our own discoveries [2, 25].

Strengths of the study included the longitudinal validation in a large number of patients, and the evaluation of the ability of the KSQ to distinguish between different patient groups.

Our cohort was less affected than the cohorts compared in previous studies [6–8, 10], as evidenced by pulmonary function tests, organ involvement and treatment requirements; thus, we have expanded the applicability of the KSQ.

The study has some limitations. The use of an additional anchor, such as the GRCS, for an overall estimation of change after 12 months could have strengthened the results. We do not view recall bias as a significant concern because the questionnaires used in our study cover a time frame of 2–4 weeks except for the FAS, which refers to "how you usually feel". Although the completion of the questionnaires after the consultation might have been influenced by information from diagnostic and follow-up investigations, we maintained consistency in this procedure throughout the study. Therefore, we do not believe it substantially affected the results, as any potential influence could have been in either direction. The low number of patients with skin and eye manifestations in our study did not enable full validation of the skin and eye domains. For completeness, and to facilitate cross-cultural comparisons of HRQoL outcomes in sarcoidosis research, full validation of these domains is needed.

Conclusion

This study marks an important advancement in the validation of the KSQ GHS, Lung and Medication domains by introducing known-groups validity and assessments of responsiveness over 12 months. In addition, the validation process and high validity in a cohort of patients with mild sarcoidosis is a novel contribution to the existing literature on the KSQ.

The KSQ demonstrated good reliability, validity and responsiveness, suggesting that it is a robust instrument for assessing HRQoL in sarcoidosis patients. The performance of KSQ in a Danish population aligns well with findings from previous studies in different populations, thus highlighting its versatility across diverse cultural and linguistic settings.

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