

## Quality of Life and Health Status in Sarcoidosis: A Review of the Literature

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Sarcoidosis is a disease associated with a wide range of symptoms, such as cough, dyspnea on exertion, chest pain, wheezing, fever, weight loss, arthralgia, and general weakness [1,2]. An increasing number of studies have shown that fatigue is a major problem for patients [2–6]. These symptoms may negatively influence patients' quality of life (QOL) [6]. QOL is an important outcome measure of treatment, especially with regard to chronic diseases. It is a concept that concerns patients' evaluation of their functioning in a wide range of domains, but always the physical, psychologic, and social domain [7]. When only these three domains are assessed, one measures health-related QOL. QOL is often confused with health status (HS), which concerns patients' physical, psychologic, and social functioning [8,9]. This article focuses on what is known about the QOL and HS of sarcoidosis patients. For the purpose of clarity, studies on QOL and HS are presented separately.

### Methods

A search using the PubMed database was performed with the key words “sarcoidosis and health status,” “sarcoidosis and quality of life,”

and “sarcoidosis and fatigue” for the time period until November 2007. This resulted in 22, 68, and 105 papers, respectively. Only 15 of the papers with the key words “fatigue” and “sarcoidosis” seemed to be relevant studies; the others mainly were case reports or reviews. Fifteen papers found with the key words “sarcoidosis” and “health status” and 14 of “fatigue” and “sarcoidosis” overlapped with the other search. From the remaining 76 papers, 17 were reviews and not included in this article, resulting in 59 papers. These papers were further reduced to 35 based on the title or abstract. Reasons for excluding papers were language (ie, not written in English, German, or Dutch; N = 11); no pulmonary sarcoidosis (N = 4); guidelines (N = 1); focus is on development or validation of questionnaires (N = 2); HS or QOL were not examined (N = 5); or not by means of questionnaires (N = 1). Finally, 24 studies resulted that directly assessed QOL, HS, or fatigue.

### Results

#### *Sarcoidosis quality of life and fatigue*

The greatest impact on QOL in sarcoidosis, as seen in clinical practice, is caused by rather nonspecific symptoms hard to objectify, such as fatigue and sleeping disorders [4]. For instance, in one study there seemed to be a number of QOL areas in which sarcoidosis patients, particularly

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those with current symptoms, experienced problems. Patients either with or without current symptoms suffered from fatigue, sleeping problems, and impaired general QOL compared with a healthy control group. Besides the physical problems mentioned previously, patients with current symptoms suffered from impaired QOL with regard to their mobility, working capacity, and activities of daily living. This was also shown in a different way in a study among Croatian sarcoidosis patients that examined the predictive value of the most frequently reported symptoms on patients QOL [7]. Fatigue, breathlessness, reduced exercise capacity, and arthralgia were the most frequently reported symptoms. Women scored lower on the domains Physical health, Psychologic health, Social relationships, and Environment, and the general facet Overall QOL. Using corticosteroids predicted a lower QOL in all domains except Spirituality. Having a partner was associated with the QOL domains Psychologic health and Level of independence, whereas a low educational level and arthralgia predicted scores on the domain Social relationships in a positive and negative way, respectively. Fatigue had a negative effect on patients' QOL domain scores for Physical health, Psychologic health, and Level of independence. Finally, diffusing capacity of lung for carbon monoxide was positively related to Spirituality [7]. In a study that focused exclusively on the relationship between fatigue and QOL, fatigue seemed to have a negative impact on all domains of QOL. In addition, the diffusing capacity for carbon monoxide was positively related to the QOL domain Level of independence, whereas gender, age, and time since diagnosis were, in various combinations, related to patients' scores on QOL domains [10]. Sarcoidosis has a considerable impact on patients' QOL, especially in those patients with current symptoms, such as fatigue. This was also shown in three other studies [11–13]. Sarcoidosis patients and rheumatoid arthritis patients had an impaired QOL compared with healthy controls. Fatigue, sleep, activities of daily living, and working capacity were major problems in both patient groups. In addition, rheumatoid arthritis patients had a worse QOL in the domains Physical health and Level of independence compared with the sarcoidosis patients [13]. Another study found that female patients have a lower QOL, except for positive feelings [12]. Finally, recent studies showed that a substantial number of sarcoidosis patients suffer from small fiber neuropathy [14]. In a case report of a patient with

severe small fiber neuropathy, high scores in fatigue, and a low QOL, infliximab, an anti-tumor necrosis factor- $\alpha$  therapy, resulted in such improvement in fatigue and QOL that scores returned to normal values [15].

#### *Sarcoidosis health status*

In three studies patients had a worse HS compared with a control group [3,16,17]. In two of these studies patients scored higher on cognitive behavior, home management tasks, recreation and hobbies, sleep, social interaction, and work [3,16]. In the study by Drent and colleagues [3], sarcoidosis patient suffering from symptoms seemed to be responsible for the differences between the sarcoidosis patients and the control group. In a study among Greek sarcoidosis patients with active sarcoidosis, patients reported more dyspnea, more anxiety and depressive symptoms, and a worse HS compared with controls that visited a smoking cessation clinic [17]. In the study by Drent and colleagues [3], the patients with current symptoms reported more depressive symptoms compared with patients without current symptoms. Moreover, whereas the latter subgroup experienced more positive affect, no differences between the two sarcoidosis subgroups were found with regard to negative affect. From the HS aspects, sleep seemed to be associated with depressive symptoms in general and depressive cognitions in particular [3]. Cox and colleagues [18] found that higher scores on depressive symptoms and perceived stress were related to lower HS scores. In another study the relationship between HS and lung function, and respiratory and peripheral muscle function, was examined [16]. Patients with symptoms showed a lower maximum inspiratory pressure, maximum expiratory pressure, and respiratory muscle endurance time compared with those without symptoms. Moreover, correlations were found between respiratory muscle endurance time and the HS aspects mobility and body care and movement. The radiographic stage was related to cognitive and emotional behavior, home management, and social interaction [16]. With regard to the relationship between pulmonary function tests and dyspnea, and HS, most studies find some relationships. Yeager and colleagues [19] found that lower scores on the spirometric tests and more self-reported dyspnea was related to a diminished HS. Furthermore, a study examining the relationship between the 6-minute walk test and HS showed

that self-reported dyspnea scores were associated with fatigue scores, the walking distance, and patients' HS. Performance on the 6-minute walk test was predicted by patients' score on the activity scale of the St. George Respiratory Questionnaire, forced vital capacity, and oxygen saturation [20]. In another study self-reported dyspnea and HS was associated with forced expiratory volume in 1 second and forced vital capacity, although it depended on the questionnaires used [17]. In a smaller study [18], spirometric tests and self-reported dyspnea were unrelated to a diminished HS. Finally, Baughman and colleagues [21] examined the usefulness of fluticasone in patients with acute symptomatic pulmonary sarcoidosis. No difference was found between the fluticasone (N = 10) and the placebo group (N = 11) with regard to HS. Oral corticosteroids seemed to be associated with significant complaints, however, whereas inhaled corticosteroids were well tolerated [21].

In a study that aimed to assess the relationship between HS and physiologic impairment [22], patients with various interstitial lung diseases (ILDs) seemed to have a moderately reduced HS. As might be expected, the scores on the applied questionnaires were related to the dyspnea scores of patients and results on their pulmonary function tests.

## Discussion

This article focuses on current knowledge of the QOL, HS, and fatigue of sarcoidosis patients. QOL in sarcoidosis is impaired with respect to mobility, working capacity, and activities of daily living, especially in sarcoidosis patients suffering from fatigue and other symptoms, such as breathlessness and arthralgia. HS of sarcoidosis patients is also lower compared with healthy controls, especially in the cognitive aspects, mobility, home management, leisure activities, sleep, social interaction, and work. Patients also displayed more depressive symptoms and, related to this, a lower HS.

### *Quality of life and health status*

The authors distinguished between studies examining QOL and HS, although research often uses the term "QOL" to cover both concepts. HS concerns the impact of disease on functioning, whereas health-related QOL also reflects patients' evaluation of their functioning. It is important to make this distinction when planning and

performing intervention studies because QOL and HS measures may provide different results and different conclusions [23].

There are several differences between the types of questions and the meaning of the scores from QOL and HS measures. First, HS may indicate whether there are limitations or not, whereas QOL also reflects to what extent patients experience these limitations as a problem in daily life. Individual expectations regarding health, the ability to cope with limitations, and the threshold for the tolerance of discomfort modulate objective HS facts into subjective values, which represents one's QOL [24]. Consequently, two persons with identical restrictions in functioning (HS) may evaluate these restrictions (QOL) differently. Similarly, a low HS score can coincide with a high score on the corresponding domain of a QOL measure within the same person. Using a HS measure to assess QOL can provide misleading conclusions [25]. This can be illustrated using the social domain. HS measures focus on how often and to what extent physical health and emotional problems have interfered with unspecified social activities. Consequently, patients with few social contacts have a low score and are expected to have an unsatisfactory social life. A QOL measure inquires about patients' satisfaction with their social contacts. Because this is not related to the size of someone's social network, few social contacts may reflect a patient's preference.

Second, HS and QOL measures differ in the level of differentiation. In general, QOL questionnaires assess more aspects of life than HS measures in such a way that it provides more detailed information on patients' life. For example, the psychologic domain of HS measures incorporate a wide spectrum of questions, such as the frequency of feeling nervous, down, calm and quiet, depressed, and happy. Because these questions are aggregated into one score, however, this does not allow the identification of the feelings that are affected. In contrast, a QOL questionnaire assesses a broader range of separate aspects of the domain (eg, negative feelings, positive feelings, and self-esteem).

Third, HS measures only aspects that are directly related to health, whereas QOL instruments measure a broader range of aspects of patients' lives. Measuring a wider scope of aspects is important because patients may feel that aspects that are not directly health-related are very relevant to them and determine their QOL [26]. An example is financial resources, which is often

influenced by disease (eg, because patients have to reduce the number of working hours).

Fourth, HS measures are characterized by the tendency to assess infirmity or disability, rather than health [27]. Questions focus on the negative consequences of disease and disregard the positive aspects of life, which are part of QOL measures. The choice for a QOL or HS measure depends on one's aim. In general, if information is wanted about what patients can and cannot do (functioning), a HS measure must be used. If one's interest is in how patients feel about several aspect of their life, however, a QOL measure is indicated. Using the right type of questionnaire to reach one's aim is of the utmost importance, because QOL and HS measures may provide conflicting results. Using a combination of HS and QOL measures has been suggested by several researchers.

#### *Quality of life and health status measures used in sarcoidosis*

Until now, only one QOL measure has been used in sarcoidosis: the World Health Organization Quality of Life Assessment Instrument-100 [28,29]. With regard to HS, five different measures have been used in sarcoidosis studies (Table 1). The Chronic Respiratory Questionnaire [30] is a respiratory-specific health-status measure that was originally developed for chronic obstructive pulmonary disease (COPD) patients. It measures four aspects of HS: (1) dyspnea, (2) fatigue, (3) emotional function, and (4) mastery. The questionnaire allows patients to rate the severity of dyspnea associated with individually identified activities. Contrary to the other questionnaires used in sarcoidosis, the Chronic Respiratory Questionnaire is an interviewer-assisted

questionnaire. It seems to be a reliable and valid instrument for COPD and asthma patients [22,30,31]. Chang and coworkers [32] have used the Chronic Respiratory Questionnaire in a validation study among patients with ILD, which included 10 sarcoidosis patients (20% of the total ILD group). They concluded that the Chronic Respiratory Questionnaire was not a good measure for use in ILD.

The Medical Outcome Study Short Form-36 [33] is a 36-item generic health-status measure that assesses health in eight dimensions: (1) physical functioning; (2) social functioning; (3) limitations in usual role activities caused by physical problems (role physical); (4) limitations in usual role activities caused by emotional problems (role emotional); (5) mental health; (6) vitality; (7) bodily pain; and (8) general health perception. In addition, health changes over the last year may be assessed. The Short Form-36 has been widely used and has good psychometric properties [34]. The reliability and validity have been shown to be good in a sample of patients with ILD, which included some sarcoidosis patients [32].

The Sarcoidosis Health Questionnaire [35] is a sarcoidosis-specific HS measure that consists of 29 questions covering three domains: (1) daily functioning, (2) physical functioning, and (3) emotional functioning. The reliability and validity of this questionnaire seems good [3], but further testing is needed. Unfortunately, fatigue, a major symptom of sarcoidosis, is only represented by one question that is part of a domain. Specific information on this symptom cannot be derived from the Sarcoidosis Health Questionnaire. To assess fatigue, another specific fatigue measure needs to be used.

Table 1  
Quality of life and health status questionnaires used or examined in sarcoidosis

Questionnaires	QOL/HS measure	Number of items	Required time (min)	Quality in sarcoidosis
CRQ	HS	20	20–30	Not good <sup>a</sup>
SF-36	HS	36	10	Good <sup>a</sup>
SGRQ	HS	76	15–20	Good <sup>a</sup>
SHQ	HS	29	10	Good
SIP	HS	136	20–30	Unknown
WHOQOL-100	QOL	100	15–20	Good

*Abbreviations:* CRQ, Chronic Respiratory Questionnaire; HS, health status; QOL, quality of life; SF-36, Medical Outcome Study Short Form-36; SGRQ, St. George Respiratory Questionnaire; SHQ, Sarcoidosis Health Questionnaire; SIP, Sickness Impact Profile; WHOQOL-100, World Health Organization Quality of Life Assessment Instrument-100.

<sup>a</sup> Validated in an interstitial lung diseases sample including 10 sarcoidosis patients.

The Sickness Impact Profile [36] is designed to assess sickness-related behavioral dysfunction in 12 categories:

1. Alertness behavior
2. Ambulation
3. Body care and movement
4. Communication
5. Eating
6. Emotional behavior
7. Home management
8. Mobility
9. Recreation and pastimes
10. Sleep and rest
11. Social interaction
12. Employment

It also provides summary scores for physical, psychosocial, and overall behavioral dysfunction. This questionnaire has not been validated for use in sarcoidosis.

The last questionnaire that has been used in sarcoidosis is the St. George Respiratory Questionnaire [37], a measure developed for COPD patients. It contains 76 items with weighted responses covering three components: (1) symptoms, (2) activity, and (3) impacts. The latter two states relate to the patient's current state of health. The St. George Respiratory Questionnaire seems to have good reliability and validity for COPD and asthma patients [37–39]. Moreover, this latter questionnaire was considered a good respiratory-specific measure useful in ILD patients, including 10 sarcoidosis patients [32].

#### *Assessment of fatigue: fatigue assessment scale*

Because fatigue has a major impact on QOL in sarcoidosis, establishing the extent of fatigue provides valuable insight regarding patients' QOL [6,10]. There is no objective parameter, however, for assessing fatigue in sarcoidosis [40]. A common way of assessing perceived fatigue is by means of questionnaires. The Fatigue Assessment Scale (FAS) is a promising measure for assessing fatigue in sarcoidosis patients [41]. The FAS is a 10-item questionnaire to assess fatigue (Appendix 1). The response scale is a 5-point scale (1 “never” to 5 “always”); scores on the FAS can range from 10 to 50. The FAS is based on four existing measures, among which is the facet Energy and fatigue from the World Health Organization Quality of Life Assessment Instrument-100, a measure previously used in the authors' fatigue studies among sarcoidosis patients. A group of 134 Dutch sarcoidosis patients

had a significantly higher FAS score compared with a representative sample of the Dutch population ( $N = 1893$ ). Furthermore, most (80%) of the general population sample scored below the cut-off score of the FAS, whereas 80% of the sarcoidosis patients scored above that score. Moreover, FAS scores seemed not to be related to lung function test results [41]. The reliability and validity of the FAS seemed to be good in persons working at least 20 hours per week and in sarcoidosis patients [41,42].

#### *Current shortcomings*

There is a lack of prospective follow-up studies focusing on QOL. Except for the intervention studies, current studies are cross-sectional in nature. Impact on life assessed with QOL measures is an important factor in predicting medical consumption. Appropriate management of sarcoidosis is mandatory because it predominantly affects young adults. Accordingly, the complicated nature of sarcoidosis underlines the need of multidisciplinary evaluation, management, and patient care that pays attention to somatic and psychosocial aspects of the disease.

#### *Clinical implications*

Beside physical problems, sarcoidosis has a substantial impact on QOL. There exists no effective treatment for fatigue in sarcoidosis. In a study examining fatigue in two groups of sarcoidosis patients, it seemed that in the group of patient members of the Dutch Sarcoidosis Society, patients using prednisone exhibited higher fatigue scores than patients not using prednisone. In the out-patient group, fatigue was unrelated to prednisone use [40,41]. Several case reports of sarcoidosis patients treated with anti-tumor necrosis factor- $\alpha$  showed a dramatic reduction in fatigue [15]. The positive effect of anti-tumor necrosis factor- $\alpha$  on fatigue has also been demonstrated in other diseases, such as Crohn's disease and rheumatoid arthritis [43,44]. These kinds of drugs, however, cannot be given to patients who are suffering exclusively from fatigue without other evidence of disease activity. Moreover, management of the patient with fatigue requires more than prescribing drugs. It is important for the physician to listen to the patient; it is wise to take seriously what the patient says. Furthermore, patients should be instructed to lead as active and involved a life as possible. Sleeping problems should be treated appropriately [45,46].

When fatigue has a partly psychologic cause, various treatments are available. Patients with clinical depression can be prescribed antidepressants. Some patients may require help to improve coping and self-management of their disease to increase their QOL. Cognitive therapy may be indicated to treat coping problems or stress perception. Furthermore, physical training programs guided by physiotherapists might also improve patients' exercise tolerance and physical fitness [47]. Because what patients can handle is clearly decreased, however, the activities should be adapted accordingly and rehabilitation programs should be developed carefully.

Furthermore, it is very important to guide persons involved in the follow-up of patients with sarcoidosis. It is important to educate employers and physicians who decide about such issues as sick

leave that the absence of objective parameters does not always guarantee that persons are healthy.

### Summary

The QOL and HS are impaired in patients suffering from sarcoidosis, especially in those with clinical symptoms. Fatigue is an integral part of the clinical picture of sarcoidosis. Although fatigue is a well-known symptom of sarcoidosis, it remains an underestimated problem in clinical practice. Objective test results, such as chest radiographs and laboratory parameters, do not always correlate with the well-being of the patient. Present studies are generally cross-sectional. There is a need for prospective follow-up studies assessing the natural course of patients' disease in relation to symptoms and QOL.

## Appendix 1

### Fatigue Assessment Scale

The following ten statements refer to how you usually feel. Per statement you can choose one out of five answer categories, varying from never to always. 1 = never, 2 = sometimes; 3 = regularly; 4 = often and 5 = always

		Never	Sometimes	Regularly	Often	Always
1.	I am bothered by fatigue	1	2	3	4	5
2.	I get tired very quickly	1	2	3	4	5
3.	I don't do much during the day	1	2	3	4	5
4.	I have enough energy for everyday life <sup>a</sup>	1	2	3	4	5
5.	Physically, I feel exhausted	1	2	3	4	5
6.	I have problems to start things	1	2	3	4	5
7.	I have problems to think clearly	1	2	3	4	5
8.	I feel no desire to do anything	1	2	3	4	5
9.	Mentally, I feel exhausted	1	2	3	4	5
10.	When I am doing something, I can concentrate quite well <sup>a</sup>	1	2	3	4	5

Based on large representative samples of the Dutch population, the cut-off score of the FAS is 21, ie, scores of  $\geq 22$  are considered to represent substantial fatigue.

<sup>a</sup> Scores on questions 4 and 10 should be recoded (1 = 5; 2 = 4; 3 = 3; 4 = 2; 5 = 1). Subsequently, the total FAS score can be calculated by summing the scores on all questions (the recoded scores for questions 4 and 10). For a digital version see [http://www.ildcare.eu/pages/artsen\\_informatie\\_fasen.html](http://www.ildcare.eu/pages/artsen_informatie_fasen.html).

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