

## Quality of life and health status in sarcoidosis

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

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## ABSTRACT

The aim of this review is to provide information on the influence of sarcoidosis on patients' quality of life (QOL) and health status (HS), a related concept. A search in the PubMed database was performed with the key words *sarcoidosis* and *health status* and *sarcoidosis* and *quality of life*. After removing double hits, reviews, articles written in a language other than English or Dutch, guidelines, articles focusing on questionnaire development or validation, and articles in which QOL or HS was not assessed, 28 articles were left for inclusion in the present review. The HS and QOL of sarcoidosis patients is negatively affected by the disease. Symptoms have an additional negative impact on patients' lives. Sarcoidosis has a substantial impact on patients' HS and QOL. Present observational studies all have a cross-sectional design. Prospective longitudinal follow-up studies are lacking, which makes inferences about cause and consequences difficult.

**KEYWORDS:** Sarcoidosis, quality of life, health status, review

Sarcoidosis is a disease with a peak incidence between 20 and 40 years.<sup>1</sup> The clinical course of sarcoidosis is highly variable and almost every organ can be involved. In more than 90% of sarcoidosis patients the lungs are affected. Furthermore, the lymph nodes, skin, and eyes are frequently involved. Patients with pulmonary sarcoidosis may present with symptoms related directly to the chest such as coughing, dyspnea on exertion, chest pain, chest discomfort, and wheezing. Other symptoms, such as fever, anorexia, weight loss, general weakness, and pain, are also attributable to sarcoidosis.<sup>2,3</sup> Several studies showed that fatigue is a prominent feature of sarcoidosis.<sup>3-6</sup> All symptoms are disabling for the patient and cause an impaired quality of life (QOL). This review discusses the influence of sarcoidosis on patients' QOL and health status (HS), a related concept. Before presenting the outcomes of studies, the concept of QOL and its uses are discussed.

## QUALITY OF LIFE

### Definition

Quality of life (QOL) is viewed as an important addition to the traditional medical end point, such as forced vital capacity (FVC), chest x-ray features, and mortality.<sup>7</sup> The fact that medical parameters are rarely associated with how patients feel plays a substantial role. Those parameters do not reflect the patients' disability appropriately. However, researchers still try to find a substantial relation between biomedical parameters and QOL.

Initially, end points focused on biomedical measures, such as forced expiratory volume in 1 second (FEV<sub>1</sub>) in pulmonary diseases, or the patient's general physical function was assessed. This constitutes functional status (see Fig. 1). Subsequently, in line with the World Health Organization (WHO) definition of health,<sup>8</sup> attention shifted toward the influence of disease

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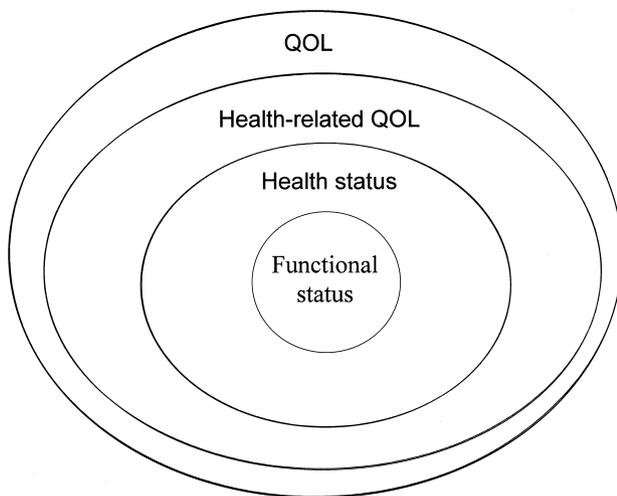
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**Figure 1** Relationship between quality of life and related concepts.

on physical, psychological, and social functioning of patients. Can someone walk stairs, buy groceries, or have some social contacts? Answers to these questions reflect HS.<sup>7,9-11</sup> In many studies the term *health-related QOL (HRQOL)* is used, when in fact it is HS that is being measured. The confusion between these two concepts originates from the fact that both assess the three domains that are directly related to health. However, HRQOL is QOL, but restricted to the physical, psychological, and social domains (see Fig. 1).

QOL is a broader concept than HS because it also contains additional domains, such as environment and spirituality.<sup>7,11-13</sup> Furthermore, QOL is concerned not only with functioning but also with how patients feel about their functioning. The concepts are also measured differently. In HS questionnaires patients are asked only what they can no longer do, whereas in QOL questionnaires positive aspects are also approached. This means that patients are not only asked about fatigue, the negative approach, but are also asked about their energy level, the positive approach. A major disadvantage of using only a negative approach is that it can lead to a tendency to answer in the negative and can induce a negative mood.

It is sometimes said that HS questionnaires assess QOL because they are completed by patients themselves and are thus subjective. However, the word *subjective* has two meanings. On the one hand the word indeed refers to the fact that both QOL and HS questionnaires are filled out by patients. On the other hand, in the context of QOL, the word *subjective* means that patients indicate how they feel about and experience their ability to function. This meaning of the word does not apply to HS questionnaires.

It is important to realize that QOL and HS are distinct concepts because being physically impaired or seeing few people does not imply that the QOL is also

bad.<sup>13</sup> Individual expectations about health, ambitions that one can no longer realize, the capacity to cope with limitations, the tolerance threshold for discomfort, and the attitude toward disease play an important role in QOL. As a consequence, two persons can have identical restrictions in functioning (HS), but evaluate them differently, resulting in a different QOL for each.<sup>7,11</sup>

### Measuring Quality of Life and Health Status

To do good research, measurement instruments are needed. Because QOL is a subjective concept and, as indicated previously, in general does not have a relationship with biomedical parameters, questionnaires are the appropriate method. Because we also want patients to provide information about their functioning, HS should also be assessed by questionnaires. It is important that questionnaires cover the multidimensionality of QOL and HS because the diversity of experiences or functioning cannot be captured in a questionnaire covering only one dimension, such as the physical one.<sup>14</sup>

There are two types of questionnaires to assess QOL: generic and disease specific. A generic questionnaire can be completed by everyone, healthy or ill. This type of questionnaire can be used to compare the relative burden of various illnesses and the relative advantages of several treatments. Disease-specific questionnaires are developed for particular diagnostic groups or patient populations, such as cancer patients, and contain questions referring to problems that are specific to particular diseases.

Contrary to the aim of disease-specific questionnaires are some researchers' attempts to examine to what extent such questionnaires can be used in patients with another disease. An example is the St. George Respiratory Questionnaire (SGRQ),<sup>15</sup> a measure developed for patients with chronic obstructive pulmonary disease (COPD), being completed by, for example, sarcoidosis patients, even though the diseases have little in common. This movement from narrow to wide application is very undesirable because the questionnaire will not cover all aspects that are important in diseases the questionnaire is not intended for, in this case sarcoidosis.

### Questionnaires Used in Sarcoidosis Studies

#### QUALITY OF LIFE

One QOL questionnaire has been used in sarcoidosis: the World Health Organization Quality of Life assessment instrument (WHOQOL-100),<sup>16,17</sup> which is a generic, cross-culturally developed measure. The questionnaire contains 100 items assessing 24 facets of QOL within six domains (physical health, psychological health, level of independence, social relationships, environment, and spirituality/religion/personal beliefs) and a

general evaluative facet called Overall Quality of Life and General Health. The response scale is a five-point Likert scale. The psychometric properties, including sensitivity to change, of the WHOQOL-100 are good.<sup>18,19</sup> Studies among sarcoidosis patients have shown that the questionnaire is reliable and valid in the study of this disease.<sup>20</sup> Furthermore, the WHOQOL-100 appeared to be a sensitive instrument to measure fatigue—one of the most common symptoms and hardest to objectify, in sarcoidosis.<sup>6</sup>

### HEALTH STATUS

With regard to HS, several generic and disease-specific measures have been used in sarcoidosis studies. The first questionnaire used was the Sickness Impact Profile (SIP),<sup>21</sup> a measure designed to assess sickness-related behavioral dysfunction. It measures 12 categories: alertness behavior, ambulation, body care and movement, communication, eating, emotional behavior, home management, mobility, recreation and pastimes, sleep and rest, social interaction, and employment. It also provides summary scores (sums of categories) for physical, psychosocial, and overall behavioral dysfunction. The scores for both categories and summary scores are expressed as percentages of the maximum possible score of dysfunction in that particular category or set of categories. The scores range between 0 and 100, with higher scores reflecting a greater impact of the disease on the patient's life. The SIP has been used in many studies among a wide range of patient populations and its reliability and validity appear to be good.<sup>21,22</sup>

The Medical Outcomes Study 36-item short form survey (SF-36)<sup>23</sup> is a generic HS measure. It assesses health in eight dimensions: physical functioning, social functioning, limitations in usual role activities due to physical problems (role physical), limitations in usual role activities due to emotional problems (role emotional), mental health, vitality, bodily pain, and general health perception. In addition, health changes over the last year are assessed. Besides scores for each subscale, the testing yields a composite HS score on a scale from 0 to 100, where a high score indicates a good HS. The SF-36 has been used widely and has good psychometric properties,<sup>23</sup> also in interstitial lung diseases (ILDs).<sup>24</sup>

The Chronic Respiratory Questionnaire (CRQ) is a respiratory-specific HS measure that was originally developed for COPD patients.<sup>25</sup> It measures four aspects of HS: dyspnea, fatigue, emotional function, and mastery. The questionnaire allows patients to rate the severity of dyspnea associated with individually identified activities. Scores for each aspect can range from 0 to 100. Higher scores indicate a better HS. Compared with the other questionnaires used in sarcoidosis, the CRQ is an interviewer-assisted questionnaire. It appears to be a reliable and valid instrument for COPD and asthma

patients.<sup>25–27</sup> More recently, Chang and coworkers<sup>24</sup> have used the CRQ in a validation study among patients with ILD, which included only 10 sarcoidosis patients (20% of the total studied ILD group). They concluded that the CRQ was not a good measure for use in ILD.

Another lung-specific questionnaire, mentioned previously, used in sarcoidosis is the SGRQ.<sup>28</sup> It has 76 items with weighted responses belonging to three components: symptoms, activity, and impacts. The latter two states relate to the patient's current state of health. In addition, all component items are aggregated into a total SGRQ score. Scores can range from 0 to 100, with higher scores indicating poorer HS. The SGRQ appeared to have good reliability and validity for COPD and asthma patients.<sup>28–30</sup> Moreover, this latter questionnaire was considered a good respiratory-specific measure useful in ILD patients.<sup>24</sup>

A few years ago, the Sarcoidosis Health Questionnaire (SHQ),<sup>31</sup> a sarcoidosis-specific HS measure, was developed. It consists of 29 questions concerning three domains: daily functioning, physical functioning, and emotional functioning. The reliability and validity of this questionnaire have been examined and appear to be good.<sup>31</sup> With regard to sensitivity to differences, based on the number of involved organ systems, the SHQ performed better than the SF-36 and the SGRQ.<sup>31</sup>

### CHOOSING A QUESTIONNAIRE

Thus an important question when it comes to choosing a suitable questionnaire for answering a particular research question is whether the results must be compared with those of other patient groups or healthy persons. The answer to this question indicates whether a generic or a disease-specific questionnaire has to be chosen. There are several other aspects that are relevant in choosing the most suitable questionnaire for a particular study. For instance, when an intervention is aimed at a domain other than the physical, psychological, or social, the chosen questionnaire must also contain this additional domain.

Also important in choosing a questionnaire is knowing exactly what is to be measured. Is it QOL? HS? or another concept? This prevents attempts to answer a QOL questions with an HS questionnaire. Thus it is important to contemplate what one wants to measure before choosing a questionnaire. The questionnaire of choice should always be analyzed to give a proper judgment about what the questionnaire assesses: QOL or HS. Selecting a questionnaire based on frequent use in other studies or the name of an instrument is discouraged because such factors do not capture the true nature of a questionnaire.

The next consideration is very practical. How much time may it take to complete a questionnaire? This poses restrictions on the length of the questionnaire and the place where it can be completed (e.g., in the

waiting room or at home). A compromise should be made between a longer questionnaire, which usually has better reliability and measures more aspects of QOL, and the time necessary to complete it.

Also, the availability of questionnaires in one's own language and culture plays a role in the choice of a questionnaire. It is important to critically review translation procedures and the usefulness of questionnaires that are originally developed in another language and culture. A translated questionnaire can seem reliable and valid even though (1) it lacks important aspects relevant to the culture where the translated questionnaire will be applied, or (2) it contains aspects that are not relevant to the culture where the questionnaire will be applied.<sup>32,33</sup> Through, for example, individual interviews or focus groups with patients from the target population, aspects from the original version that are abundant or aspects that are lacking will be revealed.

Finally, the psychometric properties of a questionnaire are important selection criteria. Of course questionnaires with good reliability and validity should be preferred. Depending on the kind of study in which a questionnaire will be used, a good sensitivity to change is of specific importance. The results of studies in which questionnaires were used without good psychometric qualities cannot be interpreted. The use of QOL questionnaires does not have to be restricted to research. They can also be used in clinical practice and to evaluate health care policy and interventions.

## METHODS

A search using the PubMed database was performed with the key words *sarcoidosis* and *health status* and *sarcoidosis* and *quality of life*. This resulted in 19 and 55 articles, respectively. Twelve articles found with the key words *sarcoidosis* and *health status* were dropped because they also appeared in the other search. From the remaining 62 articles, 15 were reviews and were, therefore, dropped, resulting in 47 articles. These 47 articles were further reduced to 28 based on the title or abstract. Reasons for excluding articles were language (i.e., not written in English, German, or Dutch,  $n=9$ ); no pulmonary sarcoidosis ( $n=1$ ); guidelines ( $n=1$ ); focus is on (development and/or validation of) questionnaires ( $n=2$ ); and HS or QOL were not examined ( $n=5$ ) or not by means of questionnaires ( $n=1$ ).

## OUTCOME OF QUALITY OF LIFE STUDIES

Quality of life (QOL) research has a short history in sarcoidosis. The first QOL study in sarcoidosis patients was published in 1998.<sup>6</sup>

Concerning QOL, nonspecific symptoms such as fatigue and pain have an important impact on the

QOL of sarcoidosis patients.<sup>34-36</sup> For instance, in a study among Croatian sarcoidosis patients, fatigue appeared to be negatively related to the QOL domains physical health, psychological health, and level of independence. In addition, patients reporting arthralgia also appeared to experience problems with social relationships.<sup>37</sup>

In one study,<sup>6</sup> sarcoidosis patients were divided into two groups: patients with actual symptoms, such as dyspnea, cough, chest pain, arthralgia, and fatigue, and patients who were asymptomatic. There appeared to be several areas in which sarcoidosis patients, especially those with current symptoms, experienced problems. Both patient groups had sleeping problems and impaired general QOL compared with healthy controls. In addition to these physical problems, patients with current symptoms suffered from impaired QOL with regard to mobility, working capacity, and activities of daily living. Thus, in agreement with other studies, sarcoidosis has a considerable impact on patients' QOL, especially in those patients with current nonspecific symptoms<sup>34,38,39</sup> and, to a lesser extent, in patients with a relatively mild respiratory functional impairment.<sup>6</sup>

In one of these latter studies,<sup>39</sup> the QOL of sarcoidosis patients was compared with the QOL of healthy controls and rheumatoid arthritis (RA) patients. In comparison with the QOL of the healthy controls, the QOL of both patient groups was impaired with regard to the domains physical health and level of independence. The RA group scored even lower than the sarcoidosis group on overall QOL and health. Fatigue, sleep, activities of daily living, and working capacity were major problems in sarcoidosis as well as RA patients. As might be expected, RA patients demonstrated more problems related to pain and mobility.<sup>36</sup> In another study, the focus was on gender differences in experiencing QOL and symptoms.<sup>34</sup> Male and female patients with symptoms differed from each other in pain, sleep, positive feelings, appearance, mobility, and activities of daily living. Female patients had a lower QOL.<sup>34</sup> The only exception was that they felt more positive feelings. The patients in this study were all recruited through the Dutch Sarcoidosis Society (DSS); possible explanations for the gender differences could not be evaluated because relevant medical data about the patients were lacking. A group of outpatients, a group of DSS members matched with the outpatients on age and gender, and a group of DSS members matched with the outpatients on age, gender, and current symptoms were studied.<sup>38</sup> The outpatient group was on average more satisfied with their physical health. They indicated to be less bothered by pain and fatigue than the DSS members. No other QOL studies have been conducted in sarcoidosis patients. HS studies will be discussed next.

## OUTCOME OF HEALTH STATUS STUDIES

Although the relationship between HS and sarcoidosis was first examined in 1997,<sup>39</sup> substantially more studies have been performed in this area.

In two studies, patients scored higher on the SIP categories cognitive behavior, home management tasks, recreation and hobbies, sleep, social interaction, and work compared with a control group.<sup>5,39</sup> Two other studies also showed that the sarcoidosis patients had an impaired HS compared with controls.<sup>40,41</sup> In the study examining respiratory muscle endurance time correlations were found with the SIP categories mobility and body care and movement. Radiographic stage was related to the categories alertness behavior, emotional behavior, home management, and social interaction.<sup>39</sup>

In the study by Drent et al,<sup>5</sup> the differences in HS found between sarcoidosis patients and a control group were mainly caused by patients suffering from symptoms, of which fatigue appeared to be the major problem. Compared with patients without current symptoms, patients with current symptoms reported more (cognitive) depressive symptoms. Moreover, whereas patients without current symptoms experienced more positive affect, no difference between the two sarcoidosis subgroups were found with regard to negative affect. From the HS aspects, sleep appeared to be associated with depressive symptoms in general and depressive cognitions in particular.<sup>5</sup> Two studies focusing on depression in sarcoidosis found a high prevalence of 60 and 66%.<sup>42,43</sup> Increased breathlessness scores and the number of systems involved were among the risk factors for depression.<sup>43</sup> Cox and colleagues<sup>42</sup> found that higher scores on depressive symptoms and perceived stress were related to lower HS scores. In accordance with this study, a Dutch study found that depressive symptoms and perceived stress were substantially related in sarcoidosis patients and that sarcoidosis patients scored high on perceived stress.<sup>44</sup>

In another study the relationship between HS and lung function, as well as respiratory and peripheral muscle function, was examined.<sup>39</sup> Correlations were found between respiratory muscle endurance time and the HS aspects mobility and body care and movement.<sup>39</sup> Others also found skeletal muscle weakness in patients with sarcoidosis who complained of fatigue. This weakness was related to reduced HS and exercise intolerance, irrespective of age, sex, body weight, and height.<sup>41</sup>

The radiographic stage was related to cognitive and emotional behavior, home management, and social interaction.<sup>39</sup> With regard to the relationship between pulmonary function tests and dyspnea, and HS, results are inconsistent. Two studies<sup>40,45</sup> found that lower scores on the spirometric tests and more self-reported dyspnea was related to a diminished HS. In another, smaller study<sup>42</sup> those relationships were not found.

Baughman and colleagues examined the usefulness of fluticasone in patients with acute symptomatic pulmonary sarcoidosis.<sup>46</sup> All patients had an initial dose of oral corticosteroids prior to enrollment in the randomized, double-blind trial of inhaled fluticasone. No difference was found between the fluticasone ( $n = 10$ ) and the placebo group ( $n = 11$ ) with regard to HS as measured with the SF-36. However, oral corticosteroids appeared to be associated with significant complaints, whereas inhaled corticosteroids were well tolerated.<sup>46</sup> A study examining the effect of thalidomide on corticosteroid-dependent pulmonary sarcoidosis ( $N = 10$ ) found no effect of treatment on patients' HS.<sup>47</sup>

Two studies have examined the relationship between HS of patients and their socioeconomic status (SES). HS was not assessed with a standardized questionnaire, but questions were asked about activity limitations and social limitations due to physical or emotional disability. Activity limitations due to physical disability were mainly related to insurance status. Patients who reported limitations were more frequently without insurance or had public insurance. Nearly all patients with a high income reported they were not limited in activities by emotional disability. Furthermore, patients with private health insurance were more likely to report no limitations while at the same time they more often indicated they were limited in the particular kind of activity. With regard to social limitations, again patients with private insurance were more likely to report no limitations.<sup>48</sup> Thus, in general patients, with a high SES reported a better HS. The same conclusion was drawn using the data from A Case Control Etiologic Study of Sarcoidosis (ACCESS).<sup>49</sup>

HS was also evaluated among lung transplant recipients ( $n = 31$ ), including only three sarcoidosis patients.<sup>50</sup> Compared with transplant candidates, transplant recipients had increased scores on all SGRQ and SF-36 scales, except bodily pain, indicating a considerable improvement in most dimensions of HS in patients who survived a lung transplant.

## DISCUSSION

This review provides information on the influence of sarcoidosis on patients' QOL and HS. In the literature, two distinct concepts are examined under the heading *quality of life*: HS and QOL. Whereas HS concerns the impact of disease on functioning (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 produce different results and thus different conclusions.

The WHOQOL-100 appears to be a good measure of QOL. There are several generic and disease-specific HS measures that have been used in sarcoidosis,

of which the SF-36 and the SHQ appear the best, although the latter still needs further testing for its use in at least other cultures and languages.

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. 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. Socioeconomic status appeared to be related to the severity of sarcoidosis and the functional limitations of patients. There is a paucity of prospective follow-up studies focusing on QOL. Except for the intervention studies, current studies are cross-sectional in nature.

The wide range of symptoms explains why the impact of sarcoidosis can only partly be compared with other chronic respiratory disorders. 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 as well as psychosocial aspects of the disease. Some patients may require help to improve coping and self-management of their disease to increase their QOL. In some cases cognitive therapy may be indicated. Physiotherapists can advise patients on how to improve their exercise tolerance and physical fitness, taking into consideration the fatigue. Rehabilitation programs should be developed to guide patients properly. Beside physical problems, sarcoidosis has a substantial impact on QOL. It is very important to guide persons involved in the follow-up of patients with sarcoidosis. Moreover, it is important to educate employers and physicians who decide about sick leave, etc. that the absence of objective parameters does not always guarantee that persons are healthy. Because what patients can handle is clearly decreased, the activities should be adapted accordingly.

In conclusion, the QOL and HS of sarcoidosis patients are impaired and symptoms are a cause of the experienced problems. Fatigue appeared to be the major problem in sarcoidosis patients. Present studies are generally cross-sectional. There is a need for prospective follow-up studies that provide information on the natural course of patients' disease in relation to symptoms and QOL.

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