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Evaluation of quality of life in sarcoidosis patients

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Health-related quality of life (QOL) has become an important topic in health care. However, hardly any attention has been paid to QOL in sarcoidosis. Therefore, the aim of this study was to assess the impact of sarcoidosis on QOL. Sixty-four sarcoidosis patients completed the World Health Organization Quality of Life assessment instrument (WHOQOL-100) and the Beck Depression Inventory (BDI). For the WHOQOL-100 a matched group of healthy controls was selected. Patients were divided into two groups: group I ($n=37$) consisted of patients with actual symptoms, group II ($n=27$) consisted of asymptomatic patients. The WHOQOL-100 revealed a number of areas in which sarcoidosis patients, especially those with current symptoms, experienced problems. A major symptom in both groups of sarcoidosis patients was fatigue. No association between the facet fatigue and the domain psychological health was found. Depressive symptoms (BDI) were associated with psychological function (WHOQOL-100). No association between pulmonary function tests and QOL was found. In conclusion, this study shows that sarcoidosis has a considerable impact on the QOL of patients. The WHOQOL-100 appeared to be a sensitive instrument to measure fatigue – one of the most common symptoms in sarcoidosis – which otherwise is difficult to assess objectively.

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Introduction

Over the past two decades, health status and quality of life (QOL) have been studied for a considerable number of chronic disease conditions (1) including respiratory diseases such as asthma (2) and chronic obstructive pulmonary disease (COPD) (3–9). COPD has been associated with impaired QOL (4,6), a high incidence of depression (3,5,6) and anxiety (6). However, the relationship between the physiological parameters of severity of COPD and QOL, when present, is not strong (7–9).

With respect to sarcoidosis, no studies regarding health status or QOL were found. Depending on the severity of sarcoidosis and the organ systems involved, patients are asymptomatic or present with symptoms such as cough, dyspnoea, chest pain, skin lesions and joint and muscle pain. The wide spectrum of symptoms makes sarcoidosis only partly comparable with other chronic respiratory disorders like COPD. The greatest impact on QOL in sarcoidosis, as seen in the clinical practice, seems to be caused by symptoms such as fatigue and sleeping disorders. Fatigue is a common problem in many chronic disorders (10). Furthermore, fatigue and sleeping disorders are often associated with depression. With respect to depression in sarcoidosis, research by Klonoff and Kleinhenz suggests that sarcoidosis patients as a group do not meet the criteria for clinical depression. Awareness of bodily sensations, however, was found to be associated with more depressive symptoms and avoidance of activities when alone (11).

In sarcoidosis, QOL and the feature fatigue have not been studied. Therefore, the primary objective of this study was to evaluate the QOL of sarcoidosis patients. A broad-ranging QOL instrument, the WHOQOL-100, which also measures fatigue, was employed. A secondary objective of this study was to investigate whether fatigue and sleeping problems in sarcoidosis patients are related to depressive symptoms.

Methods

PATIENTS

The patients suffering from sarcoidosis from eight participating Dutch hospitals (Rijnstate Hospital, Arnhem; Academic Hospital St Radboud, Nijmegen; Rehabilitation Centre Dekkerswald, Nijmegen; District Hospital Middle Twente, Hengelo; St. Jans-Hospital, Weert; Maasland Hospital, Sittard; The Wever Hospital, Heerlen; and

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TABLE 1. Demographic characteristics of the studied sarcoidosis patients with separate data for patients with (group I) and without (group II) current symptoms and the control group

	Sarcoidosis patients			Control group
	Total group	Group I	Group II	
Number of cases	64	37	27	64
Gender (male/female)	37/27	21/16	16/11	37/27
Age*	42·7 ± 11·9	45·4 ± 12·8	39·0 ± 9·6	42·8 ± 12
Smoking (yes/no)	11/53	8/29	3/24	

*Data are expressed in mean ± SD.

University Hospital, Maastricht) were studied. The diagnosis of sarcoidosis was based on consistent clinical features, along with biopsy evidence of noncaseating epitheloid cell granulomas. The clinical symptoms of the respective patients varied from none (sarcoidosis detected on routine chest X-ray film) to respiratory and general constitutional symptoms or erythema nodosum and arthralgia (i.e. Löfgren's syndrome). None of the participating subjects had any medical history, which might influence the quality of life. Moreover, patients with co-morbidity were excluded. None of the patients had any anti-depressant pharmacotherapy. In order to be able to evaluate the possible impact of the reported symptoms, as well as to evaluate the quality of life in patients without reported symptoms, the patients were divided into two groups and were studied separately. Group I consisted of patients with current symptoms (n=37), whereas group II consisted of the patients without current symptoms (n=27). The mean (SD) time from diagnosis for the whole group of sarcoidosis patients was 5·0 (5·5) years. For demographic characteristics of the patients see Table 1.

PROCEDURE

Seventy-one sarcoidosis patients from the eight participating hospitals were contacted. Seven patients declined for various private reasons, but 64 patients agreed to participate after signing an informed consent. These sarcoidosis patients were studied. They completed the WHOQOL-100 and the Beck Depression Inventory (BDI). In addition, the physician asked patients about their smoking habits and whether they had any of the following symptoms: fatigue, dyspnoea, cough, arthralgia and/or erythema nodosum.

The values of the assessed pulmonary function tests were obtained from the patient record, from the visit closest to the session the questionnaires were completed.

The healthy control group was recruited in the following way: 528 persons selected at random from the zipcode book were called. Of these persons 240 indicted to be willing to participate in a study on QOL. From the group of persons who returned a completed test-booklet (n=178; 74·2%), matched healthy control subjects (n=64) were selected on the basis of gender and age (Table 1). These control persons were used in order to compare their WHOQOL-100 scores with those of the sarcoidosis patients; they did not complete the Beck Depression Inventory (BDI). The control group was divided into two groups in such a way that patients with and without current symptoms had their own matched control group. The rationale for splitting the control group was that both groups of sarcoidosis patients would have their own matched controls in case the results showed that patients with current symptoms scored significantly different with respect to QOL from the patients without current symptoms.

Both questionnaires, the WHOQOL-100 and the BDI are self-report measures. After the subjects had completed these questionnaires, a study assistant checked whether the questionnaires had been filled in completely and no questions were skipped.

PULMONARY FUNCTION TESTS

Pulmonary function measurements included the forced expiration volume in 1 s (FEV_1) (Compactbody, Jaeger, Würzburg, Germany). The best measure of three efforts was selected. All volumes are expressed as percentages of the reference values (12). The diffusing capacity for carbon monoxide (D_LCO) was measured using the single breath method (Masterlab, Jaeger, Würzburg, Germany).

Modifications in FEV_1 and D_LCO

In order to compare the FEV_1 and D_LCO levels with the quality of life scores, the values were classified according to the American Medical Association classes: (1) normal range (>80%); (2) mild decrease (60–80%); (3) moderate decrease (40–60%) and (4) severe decrease (<40%) predicted, respectively.

QUESTIONNAIRES

World Health Organization Quality of Life assessment instrument (WHOQOL-100)

The WHOQOL-100 (Dutch version) (13) is a cross-culturally developed generic multidimensional QOL measure that has been simultaneously developed in 15 centres around the world, such as in France, Russia, the U.S.A., Panama, Zimbabwe, Japan, Thailand, and The

TABLE 2. WHOQOL items from the facets energy and fatigue and sleep and rest from the domain physical health

Facet 'energy and fatigue'	How easily do you get tired? How much are you bothered by fatigue? Do you have enough energy for everyday life? How satisfied are you with the energy you have?
Facet 'sleep and rest'	Do you have any difficulties sleeping? How much do any sleep problems worry you? How satisfied are you with your sleep? How well do you sleep?

Netherlands (14). The World Health Organization Quality of Life group (WHOQOL group) has defined QOL as 'an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to their goals, expectations, standards, and concerns' (14).

The WHOQOL-100 consists of 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 (overall quality of life and general health). Table 2 gives the questions from the facets energy and fatigue and sleep and rest from the domain physical health. Each facet is represented by four items. The response scale is a five-point Likert scale (14). Except for the facets pain and discomfort, negative feelings, and dependence on medication or treatments, higher scores show a better QOL for the facet or domain. Before calculating the domain scores the scores of these three facets have to be reversed. The reliability and validity of the Dutch version of the WHOQOL are high (15). For instance, the Cronbach alphas for the separate facets range from 0·71 to 0·94 and the questionnaire makes clear distinctions between healthy and chronically ill subjects.

Beck Depression Inventory (BDI)

Depressive symptoms of the sarcoidosis patients were measured with the BDI (16). This instrument consists of statements which are grouped in 21 groups of four possible responses. Each answer is scored on a four-point Likert-type scale of 0–3. In previous studies internal consistency was mostly higher than 0·85. Bosscher *et al.* found scores ranging from 4·5 to 5·0 in a non-clinical student population (17). A patient with a total score of 15 or above was considered to have significant depressive symptoms (5). In order to control for the physical effects of the illness on mood, items referring to problems with fatigue, sleep, sexual dysfunction, eating, weight, and general health were summed and labelled the physical depression index (PDI). The remaining items were summed and labelled the cognitive depression index (CDI). Peterson *et al.* showed that this was a valid way of preventing spurious relationships in a population with end-stage renal disease (18). Internal consistency of the CDI in this sample was high (α=0·85).

STATISTICS

Data are expressed as mean ± SD and, if appropriate, as a mean with its range. In order to detect statistically significant differences between the patient groups and their control groups, data were analysed for the WHOQOL-100 with Student's *t*-tests.

The significance concerning personal characteristics was tested using χ^2 tests for categorical data and Student's *t*-tests for continuous data. Due to the number of facets in the WHOQOL-100 and thus the number of analyses examined, a probability value of less than 0·01 was considered to be statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) (19).

Results

Patients with current symptoms (n=37; group I) had also had more symptoms at the time of the initial presentation of sarcoidosis than those without current symptoms (n=27; group II).

The reported actual symptoms of the group of symptomatic patients were fatigue in 28 cases, dyspnoea in 15 cases, arthralgia in 11 cases, cough in six cases, and erythema nodosum in one. In line with this, the major symptom assessed by the WHOQOL-100 domain physical health also appeared to be fatigue.

The QOL of the patients suffering from sarcoidosis was scrutinized for the WHOQOL-100 domains and their facets, separately. Age was related to lower scores on the facet transport (r=0·37, P<0·01) and higher scores on the facet dependence on medication or treatments (r=0·34, P<0·01).

Symptomatic patients (n=37) scored significantly different from the asymptomatic patients with respect to the domain level of independence (equal variance *t*-value 4·28, P<0·001) and the facets mobility (equal variance *t*-value 3·15, P<0·01), activities of daily living (equal variance *t*-value 3·88, P<0·01), dependence on medication or treatments (equal variance *t*-value −3·29, P<0·01), working capacity (unequal variance *t*-value 4·55, P<0·01), positive feelings (equal variance *t*-value 2·79, P<0·01), and participating in and possibilities for recreation/leisure (equal

TABLE 3. WHOQOL-100 scores of the studied sarcoidosis patients with separate data for the patients with (group I) and without (group II) current symptoms and the scores for the total control group

WHOQOL-100 scores	Group I (n=37)	Group II (n=27)	Control group (n=64)
Overall Quality of Life and General Health	14·2 (3·7)	14·2 (3·7)	16·0 (2·5)§
Physical health	14·3 (2·8)	14·2 (3·4)	16·0 (1·9)‡
Pain and discomfort	9·2 (3·1)	9·1 (3·8)	9·0 (2·9)
Energy and fatigue	12·2 (3·7)	12·0 (4·5)	15·3 (2·5)‡
Sleep and rest	14·8 (3·8)	16·9 (3·6)	17·6 (2·4)§
Psychological health	14·5 (2·6)	16·1 (2·0)	15·3 (1·7)
Positive feelings†	13·8 (3·0)	15·7 (2·2)	14·6 (1·8)
Thinking, learning, memory, and concentration	14·0 (3·4)	16·1 (2·9)	14·8 (2·3)
Self-esteem	13·9 (3·0)	15·2 (2·4)	14·7 (2·0
Body image and appearance	16·1 (3·5)	17·2 (2·2)	17·0 (2·5)
Negative feelings	9·1 (3·1)	7·8 (3·0)	8·6 (2·9)
Level of independence*	13·9 (3·3)	17·2 (2·7)	17·4 (2·4)
Mobility†	15·5 (3·4)	18·0 (2·4)	17·3 (3·2)
Activities of daily living†	13·4 (3·7)	16·8 (3·3)	17·0 (2·3)
Dependence on medication and treatments†	10·0 (4·2)	6·8 (3·2)	5·8 (2·9)
Working capacity†	12·8 (4·2)	17·0 (3·3)	17·3 (2·8)
Social relationships	15·4 (2·8)	16·9 (2·5)	15·6 (2·2)
Personal relationships	15·7 (3·0)	17·1 (2·8)	16·1 (2·0
Social support	15·4 (3·6)	17·2 (2·8)	15·8 (2·4)
Sexual activity	15·2 (3·3)	16·3 (2·9)	14·6 (3·1)
Environment	15·6 (2·1)	16·9 (1·9)	15·6 (1·7)
Physical safety and security	15·7 (2·8)	16·9 (2·8)	15·5 (2·0)
Home environment	15·5 (2·9)	17·2 (2·9)	15·6 (2·6)
Financial resources	16·5 (3·2)	17·3 (2·3)	15·7 (3·1)
Health and social care: availability and quality	15·1 (2·1)	16·0 (2·7)	14·8 (2·2)
Ability to acquire new information and skills	15·5 (2·8)	16·3 (2·5)	15·5 (2·4)
Participating in and possibilities for recreation/leisure†	14·3 (3·8)	16·8 (2·9)	15·7 (2·7)
Physical environment (pollution/noise/traffic/climate)	14·7 (2·8)	15·6 (2·6)	14·9 (2·2)
Transport	17·3 (3·4)	18·9 (1·7)	17·3 (3·0)
Spirituality/religion/personal beliefs	12·8 (3·5)	13·7 (3·4)	12·7 (2·7)

Note: Student's t-tests were applied. Data are expressed as mean with SD in parentheses. Group I *vs* group II: *P<0·001, †P<0·01. Total patient group (scores not shown) *vs.* total control group: ‡P<0·001, §P<0·01.

variance t-value 2·82, P<0·01). In each case, the QOL of the patients with symptoms was lower than the QOL of the patients without symptoms (Table 3).

For these domains and facets, separate analyses were done for patients with symptoms and matched healthy control subjects, and patients without symptoms and their matched healthy control subjects, respectively.

Regarding the domain level of independence, the symptomatic patients scored lower (unequal variance t-value 5·24, df 64·4, P<0·001) than their control group. At facet level, these patients scored lower on activities of daily living (unequal variance t-value 5·43, df 59, P<0·001), and working capacity (unequal variance t-value 5·04, df 64·1, P<0·001), and higher on the facet dependency on medication or treatments (unequal variance t-value −5·12, df 62·9, P<0·001) than their matched healthy control subjects.

Patients without symptoms scored significantly different from their control subjects on the domain environment (equal variance t-value −2·95, df 52, P<0·01) and its facets home environment (equal variance t-value −2·85, df 52, P=0·01) and transport (equal variance t-value −2·75, df 52, P<0·01). With respect to these latter areas, patients scored higher than the healthy persons.

Regarding the other domains and facets, the results for symptomatic and asymptomatic patients were comparable. Therefore, the patients were treated as one group when their scores on these QOL domains and facets were compared with the matched healthy controls.

TABLE 4. Medical characteristics of the studied sarcoidosis patients with (group I) and without (group II) current symptoms

	Group I (n=37)	Group II (n=27)
Duration of disease, years*	4·4 ± 5·1	6·1 ± 5·9
FEV_1		
>80%	29	23
60–80%	8	4
D_LCO		
>80%	22	24
60–80%	12	3
40–60%	3†	—

FEV_1=forced expiration volume in 1 s; D_LCO=diffusion capacity for carbon monoxide.
*Data are expressed in mean ± SD. †P<0·01 group I *vs.* group II.

Differences between the total sarcoidosis patient group and the total healthy control group, emerged on the domain physical health (unequal variance t-value 3·79, df 102·7, P<0·001) and its facets energy and fatigue (unequal variance t-value 5·30, df 101, P<0-·001) and sleep and rest (unequal variance t-value 3·38, df 105·8, P=0·001). In general, the sarcoidosis group indicated that they felt physically less healthy and their general sense of QOL was lower.

With respect to depressive symptoms, respondents with current symptoms had significantly higher BDI scores (9·8 ± 7·8) than those without symptoms (4·3 ± 5·6; unequal variances t-value −3·27, df=61·79, P<0·01). Of the 64 patients, 12 (18%) had a BDI score of 15 or above (associated with significant depression) (5). Of those 12 cases only one belonged to the group of patients without symptoms (group II). The average score on the CDI was 3·9 ± 4·6. Univariate analysis still showed that symptomatic patients had higher CDI scores (5·2 ± 5·3) than those without symptoms (2·2 ± 3·6; P<0·01).

For the WHOQOL-100 only the domain psychological health and the facet fatigue were related to depression (P<0·01). No correlation between the facet fatigue and the domain psychological health was found.

PULMONARY FUNCTION TESTS

Pulmonary function tests of the respective patients groups are summarized in Table 4. No correlations between the WHOQOL-100 scores and the pulmonary function tests were found.

Discussion

The results of this study showed that the major problems of patients with sarcoidosis are fatigue and low levels of energy, and that these symptoms can be measured in a standardized format.

Surprisingly, both patient groups – including patients who had reported no current symptoms – suffered from fatigue, sleeping problems and impaired general quality of life compared to the healthy control group. Sarcoidosis patients who had considered themselves asymptomatic also demonstrated an impaired QOL.

A number of differences in QOL were found between the patient groups with and without current symptoms. Besides the physical problems mentioned above, patients with current symptoms suffered from impaired QOL mainly with respect to the level of independence. This area includes problems with patients' mobility, working capacity, and activities of daily living. Moreover, group I had low levels of positive feelings and problems with recreation compared with group II. The fact that symptomatic sarcoidosis patients had a poor QOL compared to asymptomatic patients is not surprising. However, the areas in which QOL of these patients were impaired indicates that sarcoidosis has a considerable impact on daily life, even in patients with a relatively mild impairment of pulmonary function tests.

Although in many disorders fatigue is a common problem (10), in sarcoidosis fatigue and loss of energy have had hardly any attention in the literature. In the present study, scores for fatigue and loss of energy were found to be similar to those of a patient population suffering from rheumatoid arthritis (20).

Depressed mood and clinical depression are known to be associated with a lower QOL (3,5,18). In agreement with Klonoff *et al.*, the sarcoidosis patients as a group did not meet the criteria for clinical depression (11). However, patients with current symptoms had higher BDI and CDI scores than asymptomatic patients. For the WHOQOL-100 only the domain psychological health was associated with depression. This indicates that patients who were less satisfied with their psychological situation were more depressed. The facet fatigue was related to depression, but not to the domain psychological health.

The association found between the psychological health of patients and depressive symptoms could be expected, irrespective of the impairment of sarcoidosis. The absence of an association between fatigue and psychological health, however, suggests that the relationship between fatigue and depression can be explained in the context of the ongoing sarcoidosis. Patients may become exhausted by the disease. Depressive symptoms, then, at least partly, are the psychological expression of exhaustion.

For several years now, evidence has accumulated that patients with depressive disorders experience more limitations in well-being and social functioning, when compared with healthy controls and patients with chronic illness. The combination of chronic illness and depressive symptoms, however, is associated with increased morbidity and impairment of social functioning (21). Recent research suggests that functional ability plays a role here. In chronic obstructive pulmonary disease (COPD), mood and attitude were found to be closely related to breathlessness (22). Kellner *et al.* found depressive symptoms to be associated with self-rated pulmonary complaints (i.e. breathlessness) (23).

COPD patients with greater distress and poorer coping had a higher probability of readmission to hospital independent of disease severity assessed by pulmonary function tests (24). In COPD, treating psychosocial aspects and improving the patient's ability to cope with the disease has been found to be an important aspect (6). In sarcoidosis, teaching patients to cope with the limitations implied by the disease, offering psychosocial support and treating depressive symptoms may also be important. Intervention research is needed to study the causal relationship between complaints and psychological factors.

No relationship between pulmonary function tests and QOL was found. These results suggest that pulmonary function tests may not be sensitive parameters for QOL in sarcoidosis. Previously, we found that health status assessed by the Sickness Impact Profile (25) did not correlate with routinely performed pulmonary function tests in a subpopulation of this patient group (26). Moreover, the majority of patients in the present study had a normal FEV_1 and D_LCO. The limitations of this patient group, therefore, do not seem to be attributable to abnormalities in ventilatory mechanics. In our previous study mentioned above, we also found that respiratory muscle strength and endurance time was decreased in sarcoidosis patients compared to healthy controls. Moreover, a relationship was found between decreased respiratory muscle endurance time and the presence of symptoms such as fatigue (26). Future studies should focus on, in addition to respiratory symptoms, constitutional complaints such as fatigue and sleeping problems which are otherwise difficult to assess objectively.

One limitation of this study was the rather low number of patients involved, which reduces the statistical power.

In conclusion, this study shows that sarcoidosis, especially in symptomatic patients, has a considerable impact on quality of life. Rather vague symptoms like fatigue and loss of energy as well as sleeping problems in patients with sarcoidosis can be assessed with the WHOQOL-100. Moreover, the symptom fatigue was not associated with psychological health and should be attributed to the ongoing disease. Psychological health was associated with depressive symptoms in sarcoidosis patients. Treating depressive symptoms and including psychological interventions in sarcoidosis patient care may improve QOL in these patients. Intervention research, however, is needed here.

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