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A M E R I C A N   C O L L E G E   O F
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Health-Related Quality of Life of Persons With Sarcoidosis*

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Study objectives: To describe the health-related quality of life (HRQL) and mental health of persons with sarcoidosis, as well as to assess physician-patient agreement about the presence of sarcoidosis symptoms.

Design and setting: Cross-sectional study at three university medical center outpatient pulmonary clinics.

Patients: One hundred eleven outpatients with sarcoidosis seen between March and July 2002.

Measurements: The HRQL of sarcoidosis patients was measured using generic and respiratory disease-specific forms (*ie*, Medical Outcomes Study 36-item short form survey [SF-36] and the St. George respiratory questionnaire [SGRQ], respectively). Depression was assessed using the Center for Epidemiologic Studies depression scale, and stress was assessed with the perceived stress scale four-item questionnaire. The κ-statistic was calculated to compare physician-patient agreement in assessing sarcoidosis-related symptoms.

Results: Patients had moderate-to-severe reductions across all measured domains in perceived HRQL. Those patients who were prescribed oral corticosteroids had lower scores on both the SF-36 and the SGRQ than did those patients who were not. These differences were statistically significant and clinically important. The prevalence of depression was 66%, and that of significant stress was 55%. Spirometry values (FEV_1, 82% predicted; FVC, 86% predicted) were associated neither with HRQL nor with patients' perceived sarcoidosis symptoms, although they were correlated ($r = 0.43$; $p < 0.0001$) with physicians' perceptions that patients were symptomatic. Physicians and patients had only fair agreement (κ-statistic range, 0.24 to 0.36 [by center]) in assessing perceived sarcoidosis symptoms.

Conclusions: Outpatients with sarcoidosis had global reductions in measured HRQL and mental health indexes, although patients receiving therapy with oral corticosteroids had significantly worse HRQL. Experienced physicians based their assessments of patients' sarcoidosis symptoms on measures that were not related to issues of importance to patients. HRQL measurement may provide a unique insight into the impact that sarcoidosis may have on a patient's life that is not captured in traditional physiologic measures. *(CHEST 2004; 125:997–1004)*

Key words: health status indicators; quality of life; questionnaires; sarcoidosis

Abbreviations: ACCESS = A Case-Control Etiologic Study of Sarcoidosis; CES-D = Center for Epidemiologic Studies depression scale; HRQL = health-related quality of life; MCS = mental component score; PCS = physical component score; PSS = perceived stress scale; SF-36 = Medical Outcomes Study 36-item short form questionnaire; SGRQ = St. George respiratory questionnaire

Sarcoidosis is an inflammatory granulomatous disease that is characterized by diverse organ system manifestations, a variable clinical course, and a predilection for affecting relatively young adults world-wide.[1] Most persons with sarcoidosis have spontaneous remission of their disease, although between 10% and 30% may experience chronic or progressive disease[2] that can affect physical functioning[1] and mental well-being.[3,4] Although sarcoidosis was de-

scribed nearly a century ago, there are still no validated measures of disease activity or severity, no reliable predictors of disease progression, and no therapy that definitively alters long-term outcomes such as progression to pulmonary fibrosis.[5]

Past studies[6–8] of sarcoidosis patients have evaluated outcomes primarily by focusing on pulmonary manifestations of the disease, as measured by chest radiograph appearance, spirometry values, and gas exchange. However, these clinical variables are not strongly associated with long-term outcomes,[7,9,10] do not take into consideration individual responses to physiologic impairment,[11] and fail to incorporate other body systems that may have severe dysfunction and therefore may affect patients' satisfaction with life. More importantly, these clinical measures have been found to correlate poorly with the way that patients with other chronic pulmonary diseases perceive their quality of life.[12,13]

An outcome that is especially relevant to patients with a potentially chronic disease like sarcoidosis is satisfaction with life as it is affected directly and indirectly by health and disease, or health-related quality of life (HRQL).[14] Patient-centered outcomes measurements such as HRQL are useful because they allow clinicians, who often do not predict patients' perceived HRQL accurately,[15] to better understand the unique effect that similar states of health and disease may have on an individual's perceived well-being[11] in domains such as physical, mental, social, and role functioning. This information can be valuable as clinicians counsel patients, initiate and monitor therapy, or assess overall disease severity.

Researchers in Europe have reported[3,16–18] that the HRQL of sarcoidosis patients is significantly diminished. In contrast, only 10 US sarcoidosis patients have had such measurements reported,[19] although one study[4] of 150 patients found high rates of depression. However, no study has been designed specifically to examine the HRQL of US sarcoidosis patients, who have different racial and cultural backgrounds than those of European patients[20] and therefore may experience both a more severe disease course[21] as well as unique health-care disparities that could further compromise their quality of life.[22]

Therefore, we conducted a cross-sectional study with the primary aim of evaluating the health outcomes of persons with sarcoidosis, including HRQL and mental functioning. Our secondary aim was to determine how well physicians and patients agreed on the presence and importance of patients' symptoms perceived due to sarcoidosis.

MATERIALS AND METHODS

Subjects

We recruited all consecutive outpatients with sarcoidosis presenting between March and July 2002 to one of three university medical center outpatient pulmonary clinics (*ie*, University of North Carolina at Chapel Hill, Medical University of South Carolina, and East Carolina University) for inclusion in this study. Patients were excluded from the study if they were < 18 years of age, were organ transplant recipients, had active cancer, were not fluent English speakers, or had cognitive or reading deficits that prevented completion of the questionnaire. All patients had biopsy-proven sarcoidosis.[1] One hundred fifty eligible patients were approached for inclusion in the study, and 120 patients participated after providing informed written consent. Reasons for refusal of inclusion in the study included lack of time to complete the study questionnaires, disinterest in the study, and an unwillingness to complete spirometry testing.

Study Design

We used a cross-sectional design to assess the baseline HRQL of persons with sarcoidosis. This study was part of a larger project consisting of two separate cross-sectional studies in which we developed and validated a sarcoidosis-specific HRQL questionnaire.[23] Although the participants in this current study were involved in the validation of the new questionnaire, the results we report here have not been published elsewhere.

Either a trained research nurse or a main study investigator enrolled patients at the time of their regularly scheduled clinic visit. Without assistance from any staff member, patients completed a battery of quality-of-life and mental health questionnaires, a short questionnaire addressing social and demographic factors, and the Medical Research Council dyspnea scale.[24] The Medical Research Council scale ranks breathlessness from 0 (no dyspnea) to 5 (severe dyspnea) and has been validated for use among persons with a variety of pulmonary conditions.[24] Patients were also asked to rate their values for their current health state on a scale of 0 (death) to 1 (perfect health). After the clinic visit, patients performed spirometry, including measurement of the FEV_1 and the FVC, which we have reported as a percentage of predicted values adjusted for age, gender, ethnicity, and height.[25] Spirometry testing was performed according to American Thoracic Society specifications[26] and per the usual protocol of the referring center. All patients performed spirometry within 2 weeks of the clinic visit. Most (90%) did so on the same day as the clinic appointment.

Quality-of-Life and Mental Health Questionnaires

The Medical Outcomes Study 36-Item Short Form Survey: The Medical Outcomes Study 36-item short form survey (SF-36) is a generic HRQL instrument with evidence of reliability and validity for use among persons with a variety of conditions, including COPD[27] and sarcoidosis.[19] Scores for the eight domains of the SF-36 are transformed to a 100-point scale, with higher scores indicating better HRQL.[28] For the SF-36, domain scores can be summed into a composite mental component score (MCS) and a physical component score (PCS), both of which are standardized to a mean score of 50 among healthy persons. SF-36 scores for healthy control subjects from the US population that were used in comparative analyses were derived from a sample of 193 persons aged 45 to 54 years from a larger, racially diverse, nationwide, cross-sectional study of 2,474 persons without chronic disease.[29]

The St. George Respiratory Questionnaire: The St. George respiratory questionnaire (SGRQ) is a 76-item questionnaire that has been validated among patients with a variety of pulmonary conditions[12,19,30] with three domains (symptoms, activity, and impact) and that measures the effect of pulmonary disease on a person's functioning and satisfaction with life.[12] In addition to a summary total score, each domain of the SGRQ is scored on a 100-point scale with lower scores indicating better quality of life, which is the opposite of the SF-36. We derived normal SGRQ values from a historical control group of healthy persons aged 17 to 80 years without pulmonary disease.[31]

The Center for Epidemiologic Studies-Depression Questionnaire: The Center for Epidemiologic Studies-depression questionnaire (CES-D) [the 11-item version] is an instrument that has been validated for use in general populations[32] and has been used in a previous cohort study of sarcoidosis.[4] Following the work of others,[4] we have used a cutoff score of ≥ 9 to indicate depression.

The Perceived Stress Scale: The perceived stress scale (PSS) is a four-item form that has been used in a variety of populations as a general measure of stress.[33] A score of ≥ 8 was used to define significant stress.

Physician Questionnaire: At the time of the clinic visit, each patient's regular physician completed a questionnaire that included assessments of whether the patient was currently symptomatic from sarcoidosis, of whether common medical comorbidities were present, as well as of the current extent of sarcoidosis organ involvement using the ACCESS (A Case-Control Epidemiologic Study of Sarcoidosis) organ involvement index.[34] The ACCESS form was developed by clinician members of this National Heart, Lung, and Blood Institute-sponsored multicenter sarcoidosis study[35] and can be used to document the involvement of sarcoidosis ("definite," "probable," or "possible") in any of 15 organ systems. We classified positive organ involvement with sarcoidosis if the examining physician reported definite or probable involvement based on physical examination findings, laboratory test results, or radiologic imaging findings. Most patients (ie, > 90%) were seen by the study authors (MJ, CB, YK, and JD), who together averaged 18 years of experience each in treating sarcoidosis patients. These physicians were the patients' regular physicians. No patients were recruited who were not established patients.

Statistical Analysis

We used two-sample *t* tests for variables with two categories and one-way analysis of variance tests for variables with more than two categories to compare differences in quality-of-life scores by the clinical characteristics of patients. Testing also was performed using the Wilcoxon rank sum and Kruskal-Wallis tests, although the results were similar to those obtained from parametric methods. The Pearson χ^2 test or Fisher exact test was used to determine differences between dichotomous variables. We used correlations calculated by either the Pearson or Spearman methods to evaluate baseline variables with strong relationships for evidence of collinearity. Multiple linear regression modeling was performed to test for associations between adjusted independent variables of interest and SF-36 and SGRQ scores, while likelihood ratio testing was used to simplify the model. Correction for intraclass correlation related to potential test center effect was performed by variance estimate adjustment in the linear regression model.[36] Agreement between physicians and patients regarding patients' presence of symptomatic disease was assessed using the Pearson χ^2 test and the κ-statistic,[37] which measures chance-corrected agreement. We interpreted a p value of < 0.05 as indicating statistical significance. We used two statistical software packages (Stata, version 7; StataCorp; College Station, TX; and SPSS, version 10.0; SPSS; Chicago, IL) in our analyses. The institutional review boards of the University of North Carolina at Chapel Hill, the Medical University of South Carolina, and East Carolina University approved the study protocol.

RESULTS

Patients

A total of 120 patients were enrolled in the study, although we excluded data from 9 patients with incomplete questionnaires. Table 1 demonstrates that the median patient age was 45 years (age range, 22 to 73 years). Most patients were female (78%), African-American (80%), and high school graduates (66%). Nearly all patients had pulmonary involve-

Table 1—Characteristics of Participants*

Characteristic	Value (n = 111)
Age	45 (26–65)
Female	87 (78)
Ethnicity	
African American	88 (80)
White	21 (19)
Other	2 (2)
Married	55 (50)
High school graduate	71 (66)
Insurance	
Private insurance	49 (44)
Medicaid	25 (23)
Medicare or public plan	24 (22)
None	13 (13)
Currently employed	57 (51)
≥ 1 Comorbidity	61 (55)
Health status	
Excellent or very good	12 (11)
Good	33 (30)
Fair	48 (43)
Poor	16 (14)
Perceived their illness to be serious	64 (58)
Amount sarcoidosis bothered patients in the past 2 wk	
All, most, or a good bit of the time	56 (51)
Some or a little of the time	40 (35)
None	15 (14)
Perception of sarcoidosis symptoms	
Physician	61 (59)
Patient	56 (51)
FEV_1, % predicted	82 (24–103)
FVC, % predicted	86 (37–121)
Dyspnea score	2 (0–5)
Duration of sarcoidosis, mo	71 (1–490)
Organ systems involved, No.	2 (1–6)
Pulmonary sarcoidosis	104 (94)
Extrapulmonary sarcoidosis	68 (61)
Current therapy for sarcoidosis	62 (52)
Current oral steroid use	55 (50)
Oral steroid use, mo	17 (1–240)
Other sarcoidosis medications	20 (18)

*Values given as total No. (%) or median (range).

ment (94%), although 61% had additional extrapulmonary disease. The median number of organs involved was two (range, one to five organs). Participants had median FEV_1 and FVC values that exceeded 80% predicted, although the median dyspnea score was 2 (dyspnea score range, 1 to 5), signifying at least a moderate degree of breathlessness in daily activities. Overall, 58% of patients rated their health as fair or poor, and 51% reported that they had experienced significant symptoms attributable to sarcoidosis at least a good bit of the time during the preceding 2 weeks.

Questionnaire Scores

Both generic and respiratory-specific questionnaire scores reflected patients' poor HRQL across multiple domains (Table 2). Patients had decrements in all domains of the SF-36 compared to historical healthy persons, the most significant being in physical functioning, vitality, and role limitations related to both physical and emotional problems. The mean SF-36-PCS and SF-36-MCS scores were 34 (SD, 12) and 45 (SD, 12), respectively, reflecting patients' slightly greater perceived decrement in physical ability relative to mental ability. Scores on the SGRQ reflected the significant impact of patients' respiratory symptoms on their quality of life, with a total score of 44 (SD, 23). The activity domain demonstrated the greatest deficit in HRQL, with a mean score of 59 (SD, 28), while the impact domain

showed the smallest deficit (mean score, 34; SD, 25). Sarcoidosis patients' SF-36 and SGRQ scores were significantly worse than healthy historical control subjects across all domains (p < 0.001). Although there were no differences in SF-36-MCS or SF-36-PCS scores between patients with solitary thoracic involvement vs those with extrathoracic involvement (both p > 0.1), there was a trend toward higher mean total SGRQ scores among those with additional extrapulmonary disease (p = 0.045). Furthermore, there were no differences in SF-36-MCS, SF-36-PCS, SGRQ total, and CES-D scores between African-American patients and those of other ethnicities (all p > 0.5). Persons with less than a high school education or those who were unemployed were significantly lower on the SF-36 (p < 0.01). The median scores on the CES-D and the PSS were 11 and 7, respectively, and the rates of depression and significant stress were 66% and 55%, respectively.

We were interested specifically in whether differences existed in HRQL scores between those receiving oral corticosteroids and those who were not (Table 3). Using an analysis of covariance strategy based on linear regression modeling, we found that there were statistically significant differences between groups using both the SF-36-PCS scores (mean, 31 and 37, respectively; p = 0.011) and SGRQ total scores (mean, 52 and 37, respectively; p < 0.001). These differences remained statistically significant after adjustment for other relevant variables with independent associations with these scores and simplification of the model (Table 3). Additionally, these differences in SGRQ and SF-36 scores also reflected clinically important differences in HRQL.[29,38] We found no differences in SF-36-MCS scores (p = 0.055), depression (p = 0.19), or PSS scores (p = 0.10) between groups receiving steroids and those not receiving steroids using *t* tests.

We also examined squared correlations (r^2) to understand the amount of variance, or "true score," of HRQL values that was explained by clinical variables (Table 4). Spirometry findings and total sarcoidosis organ burden were not related to either the SF-36 or SGRQ total scores (p > 0.05), although depression, stress, and patients' perceived sarcoidosis symptoms were highly correlated with both questionnaires. Interestingly, although physicians' assessments of patients' symptoms were associated with spirometry results and corticosteroid use, they were not related to either HRQL scores or patients' own perceptions of symptoms. Gender, age, ethnicity, and smoking status were not significantly related to SF-36 or SGRQ total scores (p > 0.05).

Table 2—*Questionnaire Results of Study Participants**

Questionnaire	Sarcoidosis Patients	Population Control Subjects
SF-36		
Physical functioning	43 (31)	83 (22)
Role-physical	40 (42)	80 (35)
Bodily pain	51 (27)	72 (23)
General health	43 (24)	70 (21)
Vitality	39 (24)	61 (21)
Social functioning	59 (31)	83 (21)
Role-emotional	50 (46)	82 (33)
Mental health	65 (22)	74 (18)
PCS	34 (12)	45 (10)
MCS	45 (12)	51 (10)
SGRQ		
Symptoms	48 (26)	7 (7)
Activity	59 (28)	12 (15)
Impact	34 (25)	11 (13)
Total	44 (23)	3 (5)
CES-D	11 (7–19)	
PSS	7 (5–8)	
Value for current health state	0.63 (0.28)	

*Values given as mean (SD) or median (interquartile range). Study population = 111. All comparisons between SF-36 and SGRQ scores were p < 0.001 using two-sample *t* tests.

Group	Unadjusted Score	p Value	Adjusted Score†	p Value	Adjusted Score‡	p Value
SGRQ total						
Steroid users (n = 56)	52 (45–58)	<0.0001	49 (43–56)§	0.031	48 (44–53)‖	0.011
No steroids (n = 55)	37 (31–43)		39 (33–44)		39 (35–44)	
SF36-PCS						
Steroid users (n = 56)	31 (28–34)	0.011	32 (29–35)¶	0.048	32 (29–35)#	0.044
No steroids (n = 55)	37 (34–40)		37 (34–40)		37 (34–40)	
SF36-MCS						
Steroid users (n = 56)	42 (39–46)	0.055				
No steroids (n = 55)	47 (44–50)					

*Values given as predicted HRQL scores (95% confidence intervals), unless otherwise indicated. p Values are based on β-coefficients determined by multiple linear regression.

†Indicates full model.

‡Reflects simplified model using an analysis of covariance strategy.

§Adjusted for gender, duration of disease, duration of corticosteroids use, symptoms, ACCESS organ burden, depression, stress, employment status, insurance, education, percent predicted FEV_1, percent predicted FVC, and number of sarcoidosis medications.

‖Adjusted for gender, depression, stress, employment status, insurance, and education.

¶Adjusted for gender, duration of oral corticosteroid use, symptoms, depression, stress, dyspnea, employment status, insurance, percent predicted FEV_1, and percent predicted FVC.

#Adjusted for gender, symptoms, depression, employment status, and insurance.

Symptoms Assessment Agreement

Physicians and patients had a 65% raw agreement (74 of 111 assessments) regarding the presence of symptoms related to sarcoidosis. Agreement was similar when patient groups were stratified by solitary pulmonary involvement (72% agreement) and additional extrapulmonary involvement (66% agreement). However, there was a significant difference overall in the percentage of patients who perceived themselves to be symptomatic (50%) and the percentage of patients who physicians perceived to be symptomatic (61%) using Pearson χ^2 tests (p < 0.001). We found that κ-statistic values, representing the ratio of actual and potential agreement beyond chance among the three main study clinicians (MJ, JD, and CB) and patients in rating whether or not the patient was symptomatic from sarcoidosis, were 0.36 (p = 0.04), 0.24 (p = 0.02), and 0.26 (p = 0.17), respectively, at the three sites. These κ-statistic values represented only fair agreement between physician and patient agreement in assessing perceived symptoms.[39]

Table 4—*Squared Correlations (r^2) Between HRQL Questionnaire Scores and Other Variables**

Variable	PCS	MCS	SGRQ	Dyspnea	Depress	Stress	Health	Sx Pt	Sx MD	FEV₁	FVC	Work	Steroids	Burden
PCS	1.0													
MCS	0.07†	1.0												
SGRQ	0.59	0.23	1.0											
Dyspnea	0.05†	0.01‡	0.08†	1.0										
Depress	0.18	0.58	0.32	0.03‡	1.0									
Stress	0.15	0.40	0.29	0.01‡	0.42	1.0								
Health	0.29	0.21	0.29	0.05†	0.25	0.20	1.0							
Sx-Pt	0.28	0.21	0.28	0.03†	0.29	0.12	0.20	1.0						
Sx-MD	0.03‡	0.11	0.11	0.02†	0.08†	0.06†	0.04‡	0.14	1.0					
FEV₁	<0.01‡	0.02‡	0.08†	0.01‡	0.03‡	0.02‡	<0.01‡	0.19		1.0				
FVC	<0.01‡	0.02‡	0.10	0.01†	0.01‡	0.03‡	0.02‡	0.02‡	0.15	0.76	1.0			
Work	0.16	0.10	0.19	0.01‡	0.08†	0.10†	0.13	0.08	0.10†	<0.04‡	0.04†	1.0		
Steroids	0.06	0.03‡	0.10	0.01‡	0.01†	0.03‡	0.05†	0.09†	0.36	0.13	0.09†	0.01‡	1.0	
Burden	0.01‡	<0.01‡	0.01‡	0.02‡	0.01‡	<0.01‡	0.03‡	<0.01‡	<0.01‡	0.01‡	0.01‡	0.01‡	0.01‡	1.0

*All comparisons are p < 0.001, unless otherwise indicated. Depress = depression; Sx = symptomatic rom sarcoidosis; Pt = patient perception; MD = doctor perception.

†p > 0.001 and < 0.05.

‡p > 0.05.

In the largest US study to date that has been designed specifically to assess the HRQL of sarcoidosis patients, we found significant decrements in physical, emotional, social, and role functioning of stable outpatients compared to historical population control subjects, using validated generic, respiratory-specific, and mental health questionnaires that were as prominent as those reported among survivors of ARDS,[30] patients with symptomatic AIDS,[40] persons with end-stage renal disease,[41] and persons with moderate-to-severe COPD.[31] We also found that that there is a clinically important as well as statistically significant difference in perceived HRQL between those patients treated with oral corticosteroids and those not treated with them, after adjustment for potential confounding variables. Furthermore, physicians and patients had only fair agreement about the presence and importance of symptoms attributable to sarcoidosis.

Our findings complement those from the few studies that have examined the HRQL of sarcoidosis patients. The SF-36 and SGRQ results are similar to those gathered from a group of 50 patients with interstitial lung disease, which included 10 patients with sarcoidosis,[19] and their correlation with patients' perceived health status, dyspnea measures, as well as depression. Stress scales provide further support for the validity of these questionnaires for use within this population. However, it is not clear whether these questionnaires are adequately sensitive to the multisystem problems that sarcoidosis patients may have,[23] as reflected by the low correlations between HRQL scores and the extent of organ system involvement. However, a recently developed HRQL questionnaire[23] with evidence of validity and reliability that incorporates items of importance to persons with sarcoidosis—the Sarcoidosis Health Questionnaire—was able to determine differences in HRQL based on organ burden.

The mental and emotional health concerns of stable sarcoidosis outpatients appeared to be as important as physical complaints to patients' perceived well-being. Although we observed a prevalence of depressive symptoms (66%) that was nearly identical to that reported by Chang and coworkers[4] (60%) using the CES-D, Drent et al[3] found a much lower prevalence of depression (18%) among Dutch patients using the Beck depression inventory. However, the clinical differences between the US and Dutch sarcoidosis populations, including access to health care and the different questionnaires used to assess HRQL, make these results difficult to compare.[42] Also, the levels of significant stress that participants reported is cause for concern, especially in light of evidence linking stress with a variety of physiologic, mental, and social problems.[43] Overall, nearly 60% of patients perceived their condition to be "serious" in nature, perhaps contributing to their symptoms of depression and stress.

The reasons that patients with sarcoidosis report such poor HRQL and significant mental health symptoms are likely multiple. First, patients must endure an unpredictable multisystemic disease characterized by exacerbations and remissions that has no effective therapy that is free of significant side effects.[2] Patients may have multiple complaints of fatigue, body pain, and low energy that can be difficult to assess and frustrating to manage by examining physicians.[18] As a result, these symptoms may be ineffectively addressed and treated, adversely affecting HRQL. The majority of sarcoidosis patients in our study were African-American, a group with lower average income,[44] lower perceived access to quality health care,[45] and lower satisfaction with health care,[46] in comparison with whites—all factors that are associated with worse health outcomes, than white sarcoidosis patients in the United States.[22] Although we found no differences in HRQL by ethnicity, our comparisons were limited by the predominance of a single ethnic group enrolled in the study.

It is worth noting that physicians with decades of experience treating persons with sarcoidosis had relatively poor chance-corrected agreement with patients in assessing the presence of sarcoidosis symptoms. Furthermore, there were only weak correlations between physician's assessments of symptoms and patients' HRQL scores, yet strong associations with spirometry and the prescription of corticosteroids. Although our findings may reflect patients' misinterpretations of their symptoms as being related to sarcoidosis, it is also possible that physicians may not recognize the importance to patients of problems related to sarcoidosis, including depression,[4] musculoskeletal pain,[47] stress,[48] and fatigue,[47] that may not commonly be addressed in a clinical setting. Physicians also may place more weight on the results of pulmonary laboratory tests such as chest radiographs and pulmonary function testing than on pulmonary symptoms of dyspnea, cough, wheeze, and chest pain. However, spirometry values correlated only weakly with measures of HRQL, which is similar to findings from patients with both COPD[49] and sarcoidosis.[18,23] This highlights the fact that spirometry testing is a poor measure of patients' perceived well-being. Could the correlation between corticosteroid use and physicians' perceptions of symptoms simply reflect their awareness of a treatment plan that has been enacted to address patients' symptoms? Clearly, this is a possible interpretation

of our results, although it does not explain why physicians' assessments were so poorly correlated with patients' symptoms and HRQL, yet were highly associated with spirometry results.

Limitations of our study include its cross-sectional design, which precluded the measurement of changes in HRQL over time as well as the characterization of the cumulative effect of oral corticosteroids on health outcomes. Because of the controversial effect of oral corticosteroids on long-term outcomes of sarcoidosis,[8,50] such as progression to pulmonary fibrosis, our finding that corticosteroid use was associated with worse HRQL scores will be important to examine in future prospective studies. Although we did not record the pulmonary staging of patients using the method of Scadding,[51] we did not believe that chest radiograph appearance would contribute significantly to explaining a large amount of variance in HRQL scores in light of the poor correlations found in the past between spirometry and HRQL. Readers should also be aware that we compared patients' HRQL scores to unmatched historical control subjects. Because of the dramatic differences in scores, however, we doubt that the use of a matched population would account for the global decrements in HRQL that we observed among sarcoidosis patients. Although the fact that 61% of our subjects had extrathoracic sarcoidosis may seem excessive, it was probably to be expected for several reasons. First, our patients were predominantly African-American, and such patients have a high frequency of extrapulmonary sarcoidosis relative to white patients.[35] The ACCESS study[34] of sarcoidosis, which was performed at 10 major sarcoidosis centers across the United States, found that, although 50% of patients had extrathoracic disease, only 44% of these patients were African-American. Also, this is only the second study to use the ACCESS study instrument[34] to quantify disease burden. It seems likely that the use of a template such as this to guide a clinician systematically in assessing the number of organ systems involved would result in greater quantified disease burden by virtue of some degree of prompting, although this was not formally evaluated. A final consideration is that the patients who participated in the study may have had more extensive or complicated disease than those seen elsewhere because of a tertiary care center referral bias. However, > 30% of our patients had only one organ system involved, while the majority also had normal spirometry results, suggesting that we were sampling relatively stable patients who may be similar to those seen by community-based physicians. Nonetheless, because of the significant heterogeneity that is possible among persons with sarcoidosis, we caution clinicians and researchers against assuming that our findings are easily generalizable to all populations.

In conclusion, we found that the HRQL of stable outpatients with sarcoidosis was globally diminished, while this deficit was accentuated among those receiving oral corticosteroids. Additionally, the prevalence of both depression and significant stress was high. Physicians' perceptions of patients' symptoms correlated better with spirometry values than with either patients' perceived symptoms or HRQL. We believe that these results suggest that there is a need for further interventions designed to improve the health outcomes of persons with sarcoidosis as well as to facilitate communication between physicians and their patients with sarcoidosis.[52] The use of HRQL and mental health questionnaires in the clinical setting may allow clinicians to better understand the diverse ways that sarcoidosis affects patients' lives.[23]

References

1 American Thoracic Society, the European Respiratory Society, and the World Association of Sarcoidosis and Other Granulomatous Disorders. Statement on sarcoidosis: joint statement of the American Thoracic Society, the European Respiratory Society, and the World Association of Sarcoidosis and Other Granulomatous Disorders. Am J Respir Crit Care Med 1999; 160:736–755

2 Judson MA. An approach to the treatment of pulmonary sarcoidosis with corticosteroids: the six phases of treatment. Chest 1999; 115:1158–1165

3 Drent M, Wirnsberger RM, Breteler MH, et al. Quality of life and depressive symptoms in patients suffering from sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 1998; 15:59–66

4 Chang B, Steimel J, Moller DR, et al. Depression in sarcoidosis. Am J Respir Crit Care Med 2001; 163:329–334

5 Gibson GJ. Sarcoidosis: old and new treatments. Thorax 2001; 56:336–339

6 Hunninghake GW, Gilbert S, Pueringer R, et al. Outcome of the treatment for sarcoidosis. Am J Respir Crit Care Med 1994; 149:893–898

7 Gibson GJ, Prescott RJ, Muers MF, et al. British Thoracic Society sarcoidosis study: effects of long term corticosteroid treatment. Thorax 1996; 51:238–247

8 Pietinalho A, Tukiainen P, Haahtela T, et al. Early treatment of stage II sarcoidosis improves 5-year pulmonary function. Chest 2002; 121:24–31

9 Zaki MH, Lyons HA, Leilop L, et al. Corticosteroid therapy in sarcoidosis. N Y State J Med 1987; 87:496–499

10 Israel HL, Fouts DW, Beggs RA. A controlled trial with prednisone for the treatment of sarcoidosis. Am Rev Respir Dis 1973; 107:609–614

11 Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993; 118:622–629

12 Jones PW, Quirk FH, Baveystock CM, et al. A self-complete

measure of health status for chronic airflow limitation: the St. George's Respiratory Questionnaire. Am Rev Respir Dis 1992; 145:1321–1327

13 Mahler DA, Weinberg DH, Wells CK, et al. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest 1984; 85:751–758

14 Bullinger M, Anderson R, Cella D, et al. Developing and evaluating cross-cultural instruments from minimum requirements to optimal models. Qual Life Res 1993; 2:451–459

15 Hallan S, Asberg A, Indredavik B, et al. Quality of life after cerebrovascular stroke: a systematic study of patients' preferences for different functional outcomes. J Intern Med 1999; 246:309–316

16 De Vries J, Van Heck GL, Drent M. Gender differences in sarcoidosis: symptoms, quality of life, and medical consumption. Women Health 1999; 30:99–114

17 De Vries J, Drent M, Van Heck GL, et al. Quality of life in sarcoidosis: a comparison between members of a patient organisation and a random sample. Sarcoidosis Vasc Diffuse Lung Dis 1998; 15:183–188

18 Wirnsberger RM, de Vries J, Breteler MH, et al. Evaluation of quality of life in sarcoidosis patients. Respir Med 1998; 92:750–756

19 Chang JA, Curtis JR, Patrick DL, et al. Assessment of health-related quality of life in patients with interstitial lung disease. Chest 1999; 116:1175–1182

20 Rybicki BA, Maliarik MJ, Major M, et al. Epidemiology, demographics, and genetics of sarcoidosis. Semin Respir Infect 1998; 13:166–173

21 Young RC Jr, Hackney RL Jr, Harden KA. Epidemiology of sarcoidosis: ethnic and geographic considerations. J Natl Med Assoc 1974; 66:386–388

22 Fiscella K, Franks P, Gold MR, et al. Inequality in quality: addressing socioeconomic, racial, and ethnic disparities in health care. JAMA 2000; 283:2579–2584

23 Cox CE, Donohue JF, Brown CD, et al. The Sarcoidosis Health Questionnaire: a new measure of health-related quality of life. Am J Respir Crit Care Med 2003; 168:323–329

24 Brooks SM. Surveillance for respiratory hazards. ATS News 1982; 8:12–16

25 Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. Am Rev Respir Dis 1981; 123:659–664

26 American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 1991; 144:1202–1218

27 Harper R, Brazier JE, Waterhouse JC, et al. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. Thorax 1997; 52:879–887

28 Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey: I. Conceptual framework and item selection. Med Care 1992; 30:473–483

29 Ware JE Jr, Snow KK, Kosinski M, et al. SF36: health survey manual and interpretation guide. Lincoln, RI: QualityMetric, 2000

30 Davidson TA, Caldwell ES, Curtis JR, et al. Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients. JAMA 1999; 281:354–360

31 Spencer S, Calverley PM, Sherwood Burge P, et al. Health status deterioration in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001; 163:122–128

32 Radloff L. The CES-D Scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977; 1:385–401

33 Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983; 24:385–396

34 Judson MA, Baughman RP, Teirstein AS, et al. Defining organ involvement in sarcoidosis: the ACCESS proposed instrument. Sarcoidosis Vasc Diffuse Lung Dis 1999; 16: 75–86

35 Baughman RP, Teirstein AS, Judson MA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med 2001; 164:1885–1889

36 Binder DA. On the variances of asymptotically normal estimators from complex surveys. Int Stat Rev 1983; 51:279–292

37 Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull 1968; 70:213–220

38 Jones PW, Bosh TK. Quality of life changes in COPD patients treated with salmeterol. Am J Respir Crit Care Med 1997; 155:1283–1289

39 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33:159–174

40 Bing EG, Hays RD, Jacobson LP, et al. Health-related quality of life among people with HIV disease: results from the Multicenter AIDS Cohort Study. Qual Life Res 2000; 9:55–63

41 Tsuji-Hayashi Y, Sizer Fitts S, Takai I, et al. Health-related quality of life among dialysis patients in Seattle and Aichi. Am J Kidney Dis 2001; 37:987–996

42 Curtis JR, Borson S. Examining the link between sarcoidosis and depression. Am J Respir Crit Care Med 2001; 163:306–308

43 McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998; 338:171–179

44 Andrulis DP. Access to care is the centerpiece in the elimination of socioeconomic disparities in health. Ann Intern Med 1998; 129:412–416

45 Okada LM, Sparer G. Access to usual source of care by race and income in ten urban areas. J Community Health 1976; 1:163–174

46 Henry J. Kaiser Foundation. Race, ethnicity, & family care: a survey of public perceptions and experiences. Menlo Park, CA: The Henry J. Kaiser Foundation, 1999

47 Sharma OP. Fatigue and sarcoidosis. Eur Respir J 1999; 13:713–714

48 Yamada Y, Tatsumi K, Yamaguchi T, et al. Influence of stressful life events on the onset of sarcoidosis. Respirology 2003; 8:186–191

49 Curtis JR, Deyo RA, Hudson LD. Health-related quality of life among patients with chronic obstructive pulmonary disease. Thorax 1994; 49:162–170

50 Paramothayan NS, Jones PW. Corticosteroids for pulmonary sarcoidosis. Cochrane Database Syst Rev 2000; 4:CD001114

51 Scadding JG. Prognosis of intrathoracic sarcoidosis in England. BMJ 1961; 2:1165–1172

52 Detmar SB, Muller MJ, Schornagel JH, et al. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. JAMA 2002; 288:3027–3034

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