Relationship Between Clinical Variables and Health-Related Quality of Life in Young Adult Subjects With Cystic Fibrosis

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BACKGROUND: Health-related quality of life (HRQOL) has received much attention in patients with cystic fibrosis (CF). The goal of this study was to evaluate the association between clinical, lung function, sleep quality, and polysomnographic variables with 2 HRQOL questionnaires, the shorter-version World Health Organization Quality of Life (WHOQOL-BREF) and Cystic Fibrosis Quality of Life (CFQOL) questionnaires, in adult subjects with CF. METHODS: In a cross-sectional study, 51 subjects underwent clinical evaluation and overnight polysomnography and answered WHO-QOL-BREF, CFQOL, Pittsburgh Sleep Quality Index, and Epworth Sleepiness Scale questionnaires. In addition, pulmonary function tests, 6-min walk tests, and echocardiography were performed. RESULTS: For WHOQOL-BREF scores, the sleep quality index was associated with the physical domain; the percent-of-predicted 6-min walk distance (6MWD) and sleepiness scale were associated with the psychological domain; the percent-of-predicted FEV_1 and sleep quality index were associated with the social relationship domain; and the sleep quality index was associated with the environment domain. For CFQOL scores, age at diagnosis, clinical score, and sleep quality index were associated with the physical functioning domain; the percent-of-predicted 6MWD and pulmonary arterial systolic pressure were associated with the role domain; sex and sleep quality index were associated with the vitality domain; the apnea-hypopnea index was associated with the emotional functioning domain; sex and body mass index (BMI) were associated with the body image domain; the percent-of-predicted 6MWD and sleep quality index were associated with the health perception domain; age, sex, BMI, and arousal index were associated with the weight domain; age, sex, percent-of-predicted FEV_1, percent-of-predicted 6MWD, and pulmonary arterial systolic pressure were associated with the respiratory symptom domain; and the clinical score was associated with the digestive symptom domain. CONCLUSIONS: The sleep quality index score, 6MWD, sleepiness scale score, and FEV_1 were predictors of WHOQOL-BREF scores. Age at diagnosis, clinical score, sleep quality score, 6MWD, sex, apnea-hypopnea index, BMI, current age, arousal index, FEV_1, and pulmonary arterial systolic pressure were predictors of CFQOL scores. *Key words: cystic fibrosis; quality of life; sleep disorders; respiratory function tests; 6-min walk test.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Cystic fibrosis (CF) is a progressive genetic disease that affects mainly the white population. The median predicted life expectancy for patients with CF has risen steadily in the last years. In 2012, the median predicted survival age was 41.1 y, with > 49% adults with CF reaching this age.[1] However, standard treatments are rigorous, requiring time-consuming regimens

of patient self-care. Daily management routinely involves airway clearance therapies, exercise, oral and inhaled respiratory medications, and oral supplementation with pancreatic enzymes and vitamins.[2]

Because life expectancy has improved markedly, health-related quality of life (HRQOL) research has gained substantial interest in this population. HRQOL is a multidimensional construct that encompasses physical, psychological, social, and functional domains of daily life and measures the impact of health and illness on these areas of functioning.[3] HRQOL measurement has been used in clinical trials,[4,5] and reviews[6-8] have reported on HRQOL as an outcome measurement in clinical trials in adults. HRQOL measurement can provide a standardized, valid, and reliable way to obtain a subject's perspective as to the benefits and limitation of a specific intervention.[3]

The World Health Organization Quality of Life (WHOQOL) Group developed an international cross-culturally comparable quality-of-life assessment instrument.[9] Its shorter version (WHOQOL-BREF)[10] comprises 26 items of the original instrument, which aimed to encompass the general domains of HRQOL: physical health, psychological health, social relationships, and environment. It has been used in several countries and in different populations, showing many possibilities for use in international and multicultural perspectives. Moreover, a disease-specific HRQOL questionnaire has been developed for patients with CF. The Cystic Fibrosis Quality of Life (CFQOL) questionnaire[11,12] is a validated disease-specific HRQOL measure of both physical and psychosocial aspects of health. Physical HRQOL domains include physical functioning, body image, eating disturbances, digestive symptoms, respiratory symptoms, weight, health perceptions, and vitality, whereas psychosocial domains include treatment burden and emotional, social, and role functioning.

The literature shows various factors that are associated with quality-of-life domains in subjects with CF.[13-15] Although several studies have looked at HRQOL in subjects with CF, few have investigated the impact of sleep quality and sleep-disordered breathing in daily life.[16] Nocturnal oxygen desaturation was associated with impaired HRQOL independent of the effects of lung function and awake gas exchange in stable out-patients with CF and moderate-to-severe lung disease. In addition, it is important to evaluate the HRQOL in different populations of adults with CF

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QUICK LOOK

Current knowledge

Cystic fibrosis (CF) is a progressive genetic disease affecting mainly the white population and is associated with a median survival age of 41 y. Daily disease management involves airway clearance therapies, exercise, oral and inhaled respiratory medications, and dietary supplements with pancreatic enzymes and vitamins. Factors associated with quality-of-life domains in patients with CF include physical functioning, body image, eating disturbances, digestive symptoms, respiratory symptoms, weight, health perceptions, and vitality, as well as psychosocial domains, including treatment burden, emotional, social, and role functioning.

What this paper contributes to our knowledge

In adult subjects with CF, 2 health-related quality of life (HRQOL) questionnaires were compared: the shorter-version World Health Organization Quality of Life (WHOQOL-BREF) and the Cystic Fibrosis Quality of Life (CFQOL) questionnaires. Sleep quality index score, 6-min walk distance (6MWD), sleepiness scale score, and FEV_1 were predictors of WHOQOL-BREF scores. Age at diagnosis, clinical score, sleep quality score, 6MWD, sex, apnea-hypopnea index, body mass index, current age, arousal index, and FEV_1, were predictors of CFQOL scores. These findings highlight the important role of different HRQOL measures in specific subjective health perception in subjects with CF. HRQOL together with pulmonary function, 6MWD, and sleep/sleepiness scale scores provide a global assessment of subjects with CF.

with regard to clinical, nutritional, pulmonary function, and sleep quality aspects, as well as to report international and multicultural differences. The aim of this study was to evaluate the association between clinical, nutritional, lung function, sleep quality, and polysomnographic variables with 2 quality-of-life instruments, the WHOQOL-BREF and CFQOL questionnaires, in adult subjects with CF at a large tertiary care center in southern Brazil.

Methods

Subjects

This cross-sectional study recruited subjects regularly attending the adult CF out-patient clinic at the Hospital de Clínicas de Porto Alegre in Rio Grande do Sul, Brazil. Subjects were eligible if they had a confirmed diagnosis

either by at least 2 abnormal sweat chloride tests and/or by a genetic test according to international guidelines[17] and if they were $\geq$ 16 y of age. Exclusion criteria were: pulmonary exacerbation in the previous 30 d, cardiac or neurological disease or other chronic disease that limited the study procedures, current treatment with sedative or anti-epileptic drugs, and pregnancy. The study was approved by the human research ethics committee, and informed consent was obtained from adult subjects and from the parents of subjects < 18 y old.

During the study period, 67 subjects attended the adult CF clinic at the Hospital de Clínicas de Porto Alegre. Seven subjects did not have a diagnosis of CF confirmed by sweat chloride test or genetic test. Six subjects declined to participate in the study, and 3 subjects did not undergo all study evaluations. Therefore, 51 subjects were included in the study.

Procedures

Subjects underwent a comprehensive clinical and nutritional evaluation and answered questionnaires about sleep quality and HRQOL during an out-patient clinic visit. On the following day, forced spirometry, chest radiograph, Doppler echocardiography, 6-min walk test, and overnight polysomnography were performed in this order for each subject. The researchers who performed the daytime investigations were blinded to the subjects' clinical and functional status. Demographic data (current age, sex, and age and time of diagnosis) were obtained from the subjects' medical records on the date that the questionnaires were completed.

HRQOL

HRQOL was measured using the WHOQOL-BREF[18] and CFQOL[19] questionnaires, which are Portuguese validated. The CFQOL questionnaire contains 44 questions and consists of the following domains: physical functioning, role, vitality, emotional functioning, social, body image, eating disturbances, treatment burden, health perceptions, weight, respiratory symptoms, and digestive symptoms. Response choices generally included ratings of frequency and difficulty on a 4-point scale (1 [always] to 4 [never], 1 = a lot of difficulty to 4 = no difficulty) or true/false responses (1 = very true to 4 = very false). Scores were calculated from 0 to 100 points, where higher scores in each domain represented better HRQOL. The WHOQOL-BREF is a short questionnaire of 24 items across 4 scales: physical, psychological, social relationships, and environment. Scores range from 0 to 100, with higher scores indicating better HRQOL and functioning.

Pulmonary Function Test

Pulmonary function was determined according to the spirometry protocol following the American Thoracic Society criteria.[20] FVC and pre- and post-bronchodilator FEV_1 (L and percent-of-predicted) for age, height, and sex were calculated.[21]

Clinical and Radiographic Scores

Clinical scores were obtained using the Shwachman-Kulczycki scoring system.[22] A conventional chest radiograph was obtained, and a pulmonologist blinded to subject clinical status determined the radiographic scores according to the scoring system of Brasfield et al.[23]

Echocardiography

Doppler echocardiography (ATL-HDI 5000, Advanced Technology Laboratories, Bothell, Washington) was performed by a board-certified senior echocardiographer according to international recommendations.[24] Pulmonary artery systolic pressure was obtained from the estimated tricuspid regurgitation gradient and the estimated right atrial pressure.

6-min Walk Test

The 6-min walk test was performed following a standardized protocol.[25] The total distance walked and the initial and final S_{pO_2} were recorded. The 6-min walk distance (6MWD) was expressed as percent of predicted using a reference equation for the Brazilian population.[26]

Sleep Questionnaires

The Pittsburgh Sleep Quality Index (PSQI)[27] and Epworth Sleepiness Scale (ESS)[28] questionnaires were answered by subjects on the night of the diagnostic sleep study. The PSQI is a self-administered questionnaire that assesses sleep quality and disturbance. Seven components are combined to produce a global score ranging from 0 to 21. A score of > 5 indicates sensitive and specific measures of poor sleep quality. The ESS is a validated sleep and self-administered questionnaire in which a score of > 10 indicates subjective daytime sleepiness. Both questionnaires are validated and adapted to the Brazilian Portuguese language.[29,30]

Polysomnography

Standard overnight sleep studies were performed using a computerized system (Neurofax EEG-9100, Nihon Kohden, Tokyo, Japan). Awake S_{pO_2} was estimated by calcu-

lating the mean of these values at rest, in a sitting position, and during a 5-min period of wakefulness at the beginning of the study. Sleep staging, arousal analysis, and scoring of respiratory events during sleep were performed according to the American Academy of Sleep Medicine.[31] Significant sleep desaturation was defined as an S_{pO_2} during sleep of $< 90\%$ for ≥ 5 min with a nadir of at least 85%.[32]

Statistical Analysis

Descriptive statistics (mean $\pm$ SD, range, *n*, and proportion) were calculated for characteristics of the study sample (Table 1). A separate regression model was constructed for each of the 12 CFQOL domains and 4 WHOQOL-BREF domains. Hierarchical logistic regression models with predictors added one at a time were also examined to evaluate the possible collinearity among the predictors. The predictors selected in the final model were based on both numerical and clinical importance. We first constructed regression models for each of the CFQOL and WHOQOL-BREF domains using demographic, anthropometric, and clinical data. Univariate analysis was then performed using simple linear correlations to explore the relationships between demographic, clinic, and anthropometric data and HRQOL measures (WHOQOL-BREF and CFQOL). Where a significant relationship was identified ($P < .10$), a stepwise multiple regression was performed using the CFQOL and WHOQOL-BREF scores as dependent variables and significant associated demographic, clinical, and anthropometric characteristics as independent variables. Regression analysis was performed using a level of significance of $P < .05$. All analyses were performed using SPSS 18.0 (IBM, Armonk, New York).

We calculated the sample size based on the study of Quittner et al[11] using the physical functioning CFQOL dimension and percent-of-predicted FEV_1. Considering r $= 0.42$ with a power of 80% and a level of significance of .05, 47 subjects would be needed in the study.

Results

Fifty-one clinically stable subjects with CF participated in the study; 47% were female. The mean age was 25.1 $\pm$ 8.8 y, the median age at diagnosis was 3 y, and the mean body mass index (BMI) was 20.5 kg/m². Additional clinical data and other characteristics are provided in Table 1.

Tables 2 and 3 provide descriptive statistics for the WHOQOL-BREF and CFQOL scores, respectively. The highest WHOQOL-BREF scores were obtained for the social relationship domain (71 $\pm$ 21), and the lowest for the physical health domain (63 $\pm$ 18). The highest CFQOL scores were obtained for the eating disturbance (85 $\pm$ 17) and digestive symptom (83 $\pm$ 15) domains. The lowest CFQOL

Table 1. Demographics and Clinical Characteristics of Adolescent and Adult Subjects With Cystic Fibrosis

Variable	Values
Sex, *n* (%)	
Female	24 (47.1)
Male	27 (52.9)
Age, mean $\pm$ SD y	25.1 $\pm$ 8.8
Age at diagnosis, median y (IQR)	3 (21)
Time of diagnosis, median y (IQR)	15.6 (16)
BMI, mean $\pm$ SD kg/m²	20.5 $\pm$ 2.4
Shwachman-Kulczycki score, median (IQR)	70 (15)
Pulmonary artery systolic pressure, mean $\pm$ SD mm Hg	29.7 $\pm$ 7.9
ESS score, mean $\pm$ SD	8.2 $\pm$ 3.5
PSQI score, mean $\pm$ SD	6.0 $\pm$ 3.5
Arousal index score, mean $\pm$ SD	12.1 $\pm$ 6.1
Sleep stage score, mean $\pm$ SD	
Stage 1/2 sleep	62.1 $\pm$ 11.8
Stage 3 sleep	20.0 $\pm$ 7.1
Stage REM sleep	18.3 $\pm$ 6.2
AHI, median events/h (IQR)	0.3 (0.55)
S_{pO_2}, mean $\pm$ SD %	
Awake	95.1 $\pm$ 2.5
Mean sleep	92.0 $\pm$ 3.5
Minimum sleep	85.8 $\pm$ 6.3
$S_{pO_2} < 90\%$ of predicted, mean $\pm$ SD	
% of total sleep time	22.8 $\pm$ 37.7
% of REM sleep	23.7 $\pm$ 39.2
Brasfield score, median (IQR)	14 (7)
FEV_1, mean $\pm$ SD % predicted	57.7 $\pm$ 24.7
FVC, mean $\pm$ SD % predicted	69.8 $\pm$ 23.2
6MWD, mean $\pm$ SD m	544.2 $\pm$ 133.7
6MWD, mean $\pm$ SD % predicted	84.9 $\pm$ 20.0
S_{pO_2} at rest during 6MWT, mean $\pm$ SD %	96.3 $\pm$ 2.3
S_{pO_2} at end of 6MWT, mean $\pm$ SD %	93 $\pm$ 7.6

N = 51.
IQR = interquartile range
BMI = body mass index
ESS = Epworth Sleepiness Scale
PSQI = Pittsburgh Sleep Quality Index
REM = rapid eye movement
AHI = apnea-hypopnea index
6MWD = 6-min-walk distance
6MWT = 6-min-walk test

scores were obtained for the health perception domain (53 $\pm$ 28).

To examine the relationship between clinical variables and HRQOL as indicated by the WHOQOL-BREF and CFQOL scores, we constructed multivariable linear regression models controlling for age and sex. The results of the simple and multiple linear regression analyses are shown in Tables 4 and 5.

In multiple regression models for the 4 WHOQOL-BREF domains, the PSQI score associated with a less favorable physical domain; the percent-of-predicted 6MWD (positively) and ESS score (negatively) were associated with

Table 2.   WHOQOL-BREF Scores

Domain	WHOQOL-BREF Scores
Physical health	63 ± 18
Psychological health	70 ± 15
Social relationship	71 ± 21
Environment	67 ± 13

Values are presented as mean ± SD.
WHOQOL-BREF = shorter-version World Health Organization Quality of Life

Table 3.   CFQOL Scores

Domain	CFQOL Scores
Physical functioning	55 ± 32
Role	74 ± 22
Vitality	61 ± 22
Emotional functioning	73 ± 18
Social functioning	62 ± 17
Body image	76 ± 22
Eating disturbances	85 ± 17
Treatment burden	59 ± 22
Health perceptions	53 ± 28
Weight	57 ± 37
Respiratory symptoms	60 ± 17
Digestive symptoms	83 ± 15

Values are presented as mean ± SD.
CFQOL = Cystic Fibrosis Quality of Life

the psychological domain; the percent-of-predicted FEV_1 (positively) and PSQI score (negatively) were associated with the social relationship domain; and the PSQI score was inversely associated with the environment domain. In multiple regression models for the CFQOL domains, age at diagnosis (negatively), Shwachman-Kulczycki score (positively), and PSQI score (negatively) were associated with the physical functioning domain; the percent-of-predicted 6MWD was positively associated with the role domain; male sex and PSQI score were negatively associated with the vitality domain; the apnea-hypopnea index was negatively associated with the emotional functioning domain; male sex and BMI were positively associated with the body image domain; the percent-of-predicted 6MWD was positively associated with the health perception domain; age (negatively), male sex (positively), BMI (positively), and arousal index (negatively) were associated with the weight domain; age (negatively), sex (positively), percent-of-predicted FEV_1 (positively), percent-of-predicted 6MWD (positively), and pulmonary artery systolic pressure (negatively) were associated with the respiratory symptom domain; and the Shwachman-Kulczycki score were negatively associated with the digestive symptom domain.

Discussion

This cross-sectional study evaluated HRQOL in clinically stable young adult subjects with CF at a large tertiary care center in southern Brazil using a generic questionnaire (WHOQOL-BREF) and a specific questionnaire (CFQOL). The lowest WHOQOL-BREF score was obtained for the physical health domain, and the lowest CFQOL score was obtained for the health perception domain. The PSQI score, percent-of-predicted 6MWD, ESS score, and percent-of-predicted FEV_1 were independent predictors of WHOQOL-BREF scores. Age at diagnosis, Shwachman-Kulczycki score, PSQI score, percent-of-predicted 6MWD, pulmonary artery systolic pressure, sex, apnea-hypopnea index, BMI, current age, arousal index, percent-of-predicted FEV_1, and were independent predictors of CFQOL scores.

Measures of HRQOL are also important for identifying the benefits of new treatments that are demonstrated in conventional health indexes, such as pulmonary function testing. Multiple HRQOL instruments have been used previously to describe subject-related outcomes.[11,12,33,34] In 1996, the first CF-specific quality-of-life instrument (Cystic Fibrosis Questionnaire [CFQ]) was developed,[35] and in 2006, the United States Cystic Fibrosis Foundation developed an English translation of the CFQ.[11] Increases in life expectancy for patients with CF have a strong impact on measuring HRQOL using a disease-specific instrument and a general quality-of-life instrument such as the WHOQOL-BREF questionnaire.

We obtained higher PSQI scores in this study, suggesting poor sleep quality. These higher scores were correlated with lower scores in CFQOL domains, such as physical functioning, vitality, and health perception. Regarding the WHOQOL-BREF questionnaire, we observed a correlation between 3 domains (physical, social relationships, and environment). However, Bouka et al[36] observed that higher PSQI scores correlated with lower scores in the vitality, emotional functioning, social, and role domains. Still, in relation to sleep quality, statistical analysis showed that daytime sleepiness, as evaluated by the ESS, was significantly related to the psychological domain in the WHOQOL-BREF questionnaire. The ESS scores did not significantly correlate with the CFQOL domains. The arousal index correlated only with the CFQOL weight domain.

The young adult population in this study presented with significant disease severity with low clinical scores, moderate impairment of nutritional status, poor pulmonary function, and mild reduction in exercise capacity. At baseline, we found that lung function and nutritional status were similar to those in prior studies.[11,36-38] These factors surely have had a great impact on HRQOL outcomes.

We found an association between the percent-of-predicted FEV_1 and WHOQOL-BREF and CFQOL scores.

Table 4. Simple and Multiple Linear Regression Analyses of the WHOQOL-BREF Questionnaire

WHOQOL-BREF Domain	Simple Regression	β (95% IC)	Multiple Regression	β (95% IC)	Adjusted R^2
Physical	Age, y	−0.379 (−1.344 to −0.236)*	PSQI	−0.409 (−3.580 to −0.90)*	0.35
	Age at diagnosis, y	−0.309 (−0.756 to −0.047)†			
	Shwachman-Kulczycki score	0.324 (0.080–0.897)†			
	Brasfield score	0.336 (0.230–2.115)†			
	FEV$_1$, % predicted	0.374 (0.079–0.474)*			
	6MWD, % predicted	0.261 (−0.015 to −0.492)			
	Baseline S_{pO_2}	0.304 (0.237–4.535)†			
	Pulmonary artery systolic pressure, mm Hg	−0.404 (−1.544 to −0.328)*			
	PSQI	−0.454 (−3.703 to −1.032)*			
Psychological	Age, y	−0.256 (−0.944 to 0.038)	6MWD, % predicted	0.303 (0.041–0.430)†	0.34
	Age at diagnosis, y	−0.272 (−0.605 to 0.004)	ESS	−0.281 (−2.396 to 0.126)†	
	6MWD, % predicted	0.293 (0.014–0.440)†			
	ESS	−0.386 (−2.923 to −0.543)*			
	PSQI	−0.449 (−3.125 to −0.852)*			
	AHI, events/h	−0.315 (−3.384 to −0.450)†			
Social relationships	FEV$_1$, % predicted	0.269 (−0.007 to 0.460)	FEV$_1$, % predicted	0.331 (0.047–0.512)†	0.16
	PSQI	−0.358 (−3.725 to 0.537)†	PSQI	−0.432 (−4.297 to −0.843)*	
Environment	Age, y	−0.351 (−0.890 to −0.118)†	PSQI	−0.380 (−2.386 to −0.344)*	0.18
	Age at diagnosis, y	−0.312 (−0.523 to −0.035)†			
	PSQI	−0.459 (−2.566 to 0.732)*			

The variables associated with the shorter-version World Health Organization Quality of Life (WHOQOL-BREF) domains in the simple linear regression analysis ($P < .10$) were entered into the multiple linear regression model.

* $P < .01$.
† $P < .05$.
PSQI = Pittsburgh Sleep Quality Index
6MWD = 6-min walk distance
ESS = Epworth Sleepiness Scale
AHI = apnea-hypopnea index
IC = information coefficient

Table 5. Simple and Multiple Linear Regression Analyses of the CFQOL Questionnaire

CFQOL Domain	Simple Regression	β (95% IC)	Multiple Regression	β (95% IC)	Adjusted R^2
Physical functioning	Age, y	−0.414 (−2.484 to 0.561)*	Age at diagnosis, y	−0.470 (−2.020 to 0.137)†	0.67
	Sex	−0.238 (−33.074 to 2.634)	Shwachman-Kulczycki score	0.406 (0.296–1.860)*	
	Age at diagnosis, y	−0.362 (−1.442 to 0.215)*	PSQI	−0.250 (−4.148 to 0.461)†	
	Shwachman-Kulczycki score	0.578 (0.914–2.158)*			
	Brasfield score	0.510 (1.617–4.655)*			
	FEV_1, % predicted	0.626 (0.525–1.110)*			
	6MWD, % predicted	0.454 (0.319–1.145)*			
	Baseline S_{pO_2}	0.575 (4.718–11.23)*			
	Pulmonary artery systolic pressure, mm Hg	−0.517 (−3.117 to 1.108)*			
	PSQI	−0.310 (−5.371 to 0.343)†			
	S_{pO_2} < 90% of predicted	−0.440 (−0.605 to 0.158)*			
Role	Shwachman-Kulczycki score	0.242 (−0.06 to 0.938)	6MWD, % predicted	0.333 (0.037–0.692)	0.15
	FEV_1, % predicted	0.315 (0.037–0.520)†			
	6MWD, % predicted	0.383 (0.128–0.709)*			
	Baseline S_{pO_2}	0.363 (0.897–5.926)*			
	Pulmonary artery systolic pressure, mm Hg	−0.428 (−1.906 to 0.469)*			
	S_{pO_2} < 90% of predicted	−0.265 (−0.319 to 0.007)			
Vitality	Age, y	−0.517 (−1.884 to 0.670)*	Sex	0.274 (1.753–21.769)†	0.46
	Age at diagnosis, y	−0.433 (−1.065 to 0.268)*	PSQI	−0.401 (−3.925 to 1.031)*	
	FEV_1, % predicted	0.236 (−0.038 to 0.0452)			
	Baseline S_{pO_2}	0.329 (0.539–5.586)†			
	Pulmonary artery systolic pressure, mm Hg	−0.282 (−1.530 to 0.019)†			
	PSQI	−0.533 (−4.800 to 1.796)*			
Emotional functioning	PSQI	−0.392 (−3.309 to 0.643)*	AHI, events/h	−0.349 (−3.837 to 0.507)†	0.23
	AHI, events/h	−0.436 (−4.318 to 1.105)*			
Social	Age at diagnosis, y	−0.246 (−0.651 to 0.041)	NS	NS	0.90
	Brasfield score	0.288 (0.044–1.877)†			
	FEV_1, % predicted	0.279 (0.003–0.393)†			
	6MWD, % predicted	0.243 (−0.031 to 0.456)			
Body image	Sex	0.322 (2.204–26.293)†	Sex	0.339 (2.872–27.202)†	0.23
	BMI, kg/m²	0.274 (−0.017 to 5.137)	BMI	0.298 (0.378–5.193)†	
	PSQI	−0.275 (−3.514 to 0.004)†			
	AHI, events/h	−0.258 (−4.207 to 0.148)			
Eating disturbances	Age, y	−0.304 (−1.151 to 0.060)†	NS	NS	0.22
	Age at diagnosis, y	−0.304 (−0.717 to 0.038)†			
	ESS	−0.245 (−2.647 to 0.171)			
	PSQI	−0.428 (−3.431 to 0.840)*			
	AHI, events/h	−0.258 (−3.291 to 0.122)			
	Arousal index	−0.422 (−1.942 to 0.461)*			

Table 5. Continued

CFQOL Domain	Simple Regression	β (95% IC)	Multiple Regression	β (95% IC)	Adjusted R^2
Treatment burden	Shwachman-Kulczycki score	0.301 (0.049–1.025)†	NS	NS	0.05
	Brasfield score	0.240 (−0.158 to 2.143)			
	FEV_1, % predicted	0.399 (0.119–0.581)*			
	Baseline S_{pO_2}	0.307 (0.311–5.398)†			
	Pulmonary artery systolic pressure, mm Hg	−0.372 (−1.751 to 0.289)*			
	$S_{pO_2} < 90\%$ of predicted	−0.335 (−0.352 to 0.037)†			
Health perceptions	Age, y	−0.297 (−1.823 to 0.074)†	6MWD, % predicted	0.309 (0.020–0.845)†	0.35
	Age at diagnosis, y	−0.236 (−1.024 to 0.085)			
	Shwachman-Kulczycki score	0.325 (0.123–1.374)†			
	FEV_1, % predicted	0.335 (0.074–0.687)†			
	6MWD, % predicted	0.407 (0.203–0.937)*			
	Baseline S_{pO_2}	0.429 (2.040–8.274)*			
	Pulmonary artery systolic pressure, mm Hg	−0.391 (−2.321 to 0.448)*			
	PSQI	−0.410 (−5.366 to 1.184)*			
Weight	Sex	0.442 (13.572–51.551)*	Age, y	−0.268 (−2.180 to 0.092)†	0.42
	BMI, kg/m²	0.379 (1.765–10.017)*	Sex	0.421 (13.393–48.628)*	
	Arousal index	−0.418 (−4.101 to 0.947)*	BMI, kg/m²	0.351 (1.930–8.964)*	
			Arousal index	−0.285 (−3.113 to 0.334)*	
Respiratory symptoms	Age, y	−0.340 (−1.156 to 0.133)†	Age, y	−0.290 (−0.953 to 0.144)*	0.58
	Shwachman-Kulczycki score	0.433 (0.239–0.947)*	Sex	0.274 (1.928–16.165)†	
	Brasfield score	0.379 (0.360–2.043)*	FEV_1, % predicted	0.545 (0.132–0.601)*	
	FEV_1, % predicted	0.650 (0.291–0.585)*	6MWD, % predicted	0.260 (0.036–0.396)†	
	6MWD, % predicted	0.336 (0.055–0.504)†	Pulmonary artery systolic pressure, mm Hg	−0.455 (−1.596 to 0.320)*	
	Baseline S_{pO_2}	0.540 (2.131–5.582)*			
	Pulmonary artery systolic pressure, mm Hg	−0.623 (−1.784 to 0.839)*			
	ESS	0.246 (−0.156 to 2.521)			
	$S_{pO_2} < 90\%$ of predicted	−0.422 (−0.305 to 0.072)*			
Digestive symptoms	Age, y	−0.459 (−1.218 to 0.348)*	Shwachman-Kulczycki score	−0.415 (−0.958 to 0.064)†	0.37
	Age at diagnosis, y	−0.501 (−0.796 to 0.268)†			
	BMI, kg/m²	−0.326 (−3.738 to 0.343)†			
	Shwachman-Kulczycki score	−0.410 (−0.827 to 0.182)*			
	Brasfield score	−0.298 (−1.631 to 0.067)†			
	ESS	−0.301 (−2.490 to 0.119)†			
	PSQI	−0.267 (−2.322 to 0.042)			

The variables associated with the Cystic Fibrosis Quality of Life (CFQOL) domains in the simple linear regression analysis ($P < .1$) entered into the multiple linear regression model.
* $P < .01$.
† $P < .05$.
PSQI = Pittsburgh Sleep Quality Index
6MWD = 6-min-walk distance
AHI = apnea-hypopnea index
BMI = body mass index
ESS = Epworth Sleepiness Scale
NS = not significant
IC = information coefficient

Previous studies showed that pulmonary function in adults with CF is also a significant predictor of CFQOL scores.[38,39] In a longitudinal study, Abbott et al[38] observed that the percent-of-predicted FEV_1 significantly correlated with all domains except body image. In contrast, in the present study, the percent-of-predicted FEV_1 showed an association only with the social relationship domain in the WHOQOL-BREF questionnaire and the respiratory symptom domain in the CFQOL questionnaire. When specific instruments are used, this correlation becomes more consistent. Measurement with different HRQOL instruments provides additional information on the impact of this disease that cannot be obtained by physiological tests such as pulmonary function testing.

BMI and percent-of-predicted FEV_1 are important indicators of disease status in patients with CF, and those patients with better nutritional status report a better HRQOL.[40] In the present study, there was no evidence of association between BMI and any of the WHOQOL-BREF domain scores, although BMI was a predictor of CFQOL scores. Similar results were demonstrated by Dill et al[41] in a longitudinal study with subject-reported outcomes: nutritional status was associated with CFQ-Revised physical domain scores. Our study demonstrated a significant effect for sex as a predictor of CFQOL scores for the weight and body image domains, but there were no associations with any WHOQOL-BREF scores. In a previous study, female sex was associated with higher scores in body image and weight scales, and females reported lower physical functioning and vitality scores.[39] However, Shoff et al[40] found no significant sex differences in mean CFQ dimension scores or nutritional status scores in children and adolescents, but the strength of association between nutritional status and CFQ scores differed between boys and girls for some dimensions, such as physical functioning. In the present study, the 6MWD was an independent predictor for both WHOQOL-BREF and CFQOL scores. Bradley et al[42] demonstrated that the performance in the modified shuttle test was significantly associated with the change in quality of life according to the Chronic Respiratory Disease Questionnaire.[43] The 6-min walk test is a useful measure of functional capacity, and it has been widely used to measure the response to therapeutic interventions for pulmonary disease such as CF.[44]

This study has some potential limitations that should be addressed. It is a cross-sectional study, and therefore, it is not possible to establish the temporal sequence between the factors studied and HRQOL. In addition, this investigation was done in a single center with a small sample size. Notwithstanding, the study was performed in the largest CF center in southern Brazil, and the factors identified as predictors of HRQOL would be relevant for clinical care and clinical research in CF.

Although there are several studies on the subject, our findings contribute to raising the awareness of the multifactorial aspects, including polysomnographic variables, related to HRQOL in subjects with CF, and we also evaluated 2 quality-of-life instruments (WHOQOL-BREF and CFQOL). In the attempt to improve HRQOL in clinical practice, the CF multidisciplinary team should take into account all relevant clinical, nutritional, pulmonary function, and sleep quality data under evaluation.

Conclusions

In summary, in adult subjects with CF, PSQI score, 6MWD, ESS score, and percent-of-predicted FEV_1 were independent predictors of WHOQOL-BREF scores. Age at diagnosis, Shwachman-Kulczycki score, PSQI score, 6MWD, sex, apnea-hypopnea index, BMI, current age, arousal index, percent-of-predicted FEV_1, and pulmonary artery systolic pressure were independent predictors of CFQOL scores. Therefore, the findings support the important role of different quality-of-life measures in specific subjective health perception in subjects with CF. Healthcare professionals should consider routinely evaluating HRQOL together with pulmonary function, 6MWD, and sleep/sleepiness scale scores.

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