

Health-related Quality of Life in Patients with Sleep-Related Breathing Disorder

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Abstract

Background: The aim of this study was to evaluate health-related quality of life (HrQoL) in patients with obstructive sleep apnea (OSA) and to investigate the impact of socio demographic and clinical parameters on HrQoL.

Methods: A total of 627 patients were consecutively recruited in 18 sleep laboratories in the state of Hessen, Germany. Standardized questionnaires were used to assess co-morbid disorders, depressive symptoms (Beck Depression Inventory) and daytime sleepiness (Epworth Sleepiness Scale). HrQoL was evaluated with the generic EuroQoL-Instrument (EQ-5D-3L index and EQ VAS). Influencing factors were analyzed using bivariate and multiple linear regression analyses.

Results: The mean EQ-5D-3L index was 0.86 ± 0.19 , and the mean EQ VAS score was 66.8 ± 19.3 . Patients primarily reported problems in the domains of pain/discomfort (55.5%), anxiety/depression (33.5%), and usual activities (29.5%). Multivariate analyses explained 34.9% and 35.9% of the variance in the EQ VAS and the EQ-5D-3L index, respectively. Relevant predictors of HrQoL were patient age, daytime sleepiness, the presence of medical comorbidities and depression.

Conclusions: The results of our study suggest that depressive disorders and excessive daytime sleepiness have considerable effects on patient HrQoL and should be considered in the treatment of OSA patients to improve HrQoL.

Keywords: Obstructive sleep apnea; Quality of life; Excessive daytime sleepiness; Depression

Introduction

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder characterized by intermittent apneas and hypopneas, leading to nocturnal hypoxemia, hypercapnia, arousals, and sleep fragmentation [1]. These nocturnal events negatively affect patients' daytime performance, resulting in fatigue and excessive daytime sleepiness, altered mood, diminished neurocognitive abilities, reduced work productivity as well as cardiovascular diseases [2-4]. These impairments often result in reduced functional and social capability and poor quality of life [5,6]. Due to the increasing prevalence of OSA worldwide (approximately 3-9% in women and 3-17% in men), the diagnosis and treatment of patients suffering from OSA result in high health care costs [1,7]. Therefore, OSA has a major impact on national healthcare systems. Patient-centered outcome variables, such as health-related quality of life (HrQoL), have become increasingly important in clinical and health service research. HrQoL can be defined as a multidimensional and subjective construct describing the physical, mental, and social dimensions of quality of life that immediately influence a person's health status [8].

Numerous earlier studies have explored HrQoL in patients with OSA showing poorer HrQoL compared with the general population. The associations between depression/daytime sleepiness and HrQoL have frequently been assessed using generic or disease-specific questionnaires [9,10]. Several studies found daytime sleepiness, depressive disorders and reduced sleep quality to significantly diminish HrQoL [11]. However, it remains unclear whether disease severity is significantly associated with patient HrQoL [12-14]. A longitudinal study over five years by Silva et al. did not demonstrate a relevant worsening of HrQoL according to an increase in the severity of sleep disorders [6]. Despite the importance of evaluating predictive variables of HrQoL to improve health care for patients with OSA, there is a lack of evidence for the German population. Therefore, the aim of the study was to evaluate the association between health-related quality of life (HrQoL) in OSA and sociodemographic and clinical parameters.

Methods

Study design

The study was performed in 18 (of 24) sleep laboratories accredited by the German sleep society (Deutsche Gesellschaft für Schlafmedizin, DGSM) in the state of Hessen during the 2nd quarter of 2009. Patients

with a recently diagnosed OSA and persons scheduled for the sleep laboratory for evaluation of a possible OSA were included. Enrollment in the study required an age ≥ 18 years and written informed consent. Persons suffering from dementia were excluded. In total, 627 patients were consecutively enrolled [15].

Patients and the physician of the respective sleep laboratory had to fill in questionnaires concerning sociodemographic parameters, medical comorbidities, medication, previous medical appointments, and medical costs. Additionally, questionnaires concerning patients' HrQoL (EuroQol-Instrument) [8], daytime sleepiness (Epworth Sleepiness Scale) [16], and depression (Beck's Depression Inventory) [17] were used.

Clinical measurements and patient-reported outcomes

EuroQol-Instrument (EQ-5D-3L index and EQ VAS): The generic EuroQol-instrument is widely used for the assessment of HrQoL [18]. The EQ-5D-3L index comprises five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain can be rated at three levels: no problems, some/moderate problems, and severe problems. As a result, $3^5 (=243)$ different conditions of HrQoL are computable. The single values are converted into preference-based indices with a range from -0.205 to 0.999 (indicating worst and best HrQoL, respectively) using German tariffs [8]. For an evaluation of patients' current health status, the EQ VAS was used with a minimum score of 0 points (lowest HrQoL) and a maximum score of 100 points (highest HrQoL).

Epworth Sleepiness Scale (ESS): The Epworth Sleepiness Scale (ESS) is a widely used, self-administered instrument for the assessment of daytime sleepiness, including in patients with sleep-related breathing disorders [16]. The ESS comprises eight questions that are answered on a four-point Likert scale (0-3), with a maximum score of 24 points and higher scores indicating a greater chance for daytime sleepiness. Patients are asked to estimate the probability to doze off or to fall asleep during eight different usual daily activities.

Beck Depression Inventory (BDI-II): The presence of depressive symptoms was evaluated using the second edition of the Beck Depression Inventory (BDI-II) [17], assessing depression in its cognitive, behavioral, emotional, and physical dimensions. The BDI-II consists of 21 items, which were self-rated by the patient on a scale from 0 to 3 points, with a maximum score of 63. In accordance with

previous studies, patients were divided into five severity groups by means of the BDI-II sum score: no depression (0-8 pts.), minimal depression (9-13 pts.), mild depression (14-19 pts.), moderate depression (20-28 pts.), or severe depression (>28 pts.) [19].

Data entry and statistical analysis: Statistical analyses were performed using Microsoft Office Excel 2003 (Microsoft Corporation, Redmond, USA) and SPSS Version 22.0 (IBM SPSS Statistics, Armonk, USA). All data are presented as means with standard deviation (SD) or number of cases (percentages) as appropriate. Differences between indicated groups were investigated using parametric and non-parametric tests. A significance level of $\alpha=0.05$ was defined to determine associations between HrQoL and different parameters such as socio-demographic and clinical data. For the comparison between two groups, t-tests and Mann-Whitney U-tests were used. Comparisons of more than two groups were performed using the Kruskal-Wallis test and an analysis of variance (F-test). To control for confounding effects, independent predictors of HrQoL were assessed using multivariate linear regression analyses with the EQ-5D-3L index and the EQ VAS score as dependent variables. Therefore, we selected variables using Spearman's rank correlation or Pearson's test with regard to their possible impact on patients' HrQoL. Afterwards, multivariate linear regression analyses were performed to detect unique contributions to the explanation of the criterion variables.

Ethical approval: The study was approved by the local ethics committee of the Philipps-University of Marburg (Approval-No. 195/07). After screening for inclusion, potential participants were informed of the aims, the content, and the protocol of the study. Informed consent was obtained from all individual participants included in the study.

Results

Socio-demographic and clinical characteristics of the sample

The clinical and socio-demographic characteristics of the study sample are provided in Table 1. Among the 627 study completers, the majority (80.2%) was male; the mean age was 56.1 ± 11.8 years (range 20-89 years). Female participants were significantly older than male patients ($p<0.001$). Half of the patients worked as employee full-time or part-time. Additionally, 5.7% of the participants were unable to work, and 8.5% of the participants were prematurely retired.

	Total	Female	Male
	mean \pm SD	mean \pm SD	mean \pm SD
Age (years)	56.1 \pm 11.8	60.1 \pm 12.1	55.2 \pm 11.5
	n (%)	n (%)	n (%)
	627 (100.0)	124 (19.8)	503 (80.2)
Family status			
Living in a relationship	502 (80.1)	85 (68.5)	417 (82.9)
Not living in a relationship	123 (19.6)	38 (30.6)	85 (16.9)
Employment situation			
Employee	312 (49.8)	43 (36.7)	269 (53.5)

Self-employed	61 (9.7)	7 (5.6)	54 (10.7)
Old-age pension	146 (23.3)	45 (36.3)	101 (20.1)
Gross Income (per month)			
less than 1700 Euros	57 (9.1)	21 (16.9)	36 (7.2)
more than 1700 Euros	286 (45.6)	28 (22.6)	285 (56.7)
Health Insurance			
Statutory	541 (86.3)	115 (92.7)	426 (84.7)
Private	80 (12.8)	8 (6.5)	72 (14.3)
Comorbidities			
Hypertension	357 (56.9)	81 (65.3)	276 (54.9)
Diabetes mellitus type II	75 (12.0)	16 (12.9)	59 (11.7)
Thyroidal diseases	66 (10.5)	28 (22.6)	38 (7.6)
Cardiac arrhythmia	62 (9.9)	16 (12.9)	46 (9.1)
Pulmonary diseases	59 (9.4)	10 (8.1)	49 (9.7)
Musculoskeletal diseases	53 (8.5)	19 (15.3)	34 (6.8)
COPD	52 (8.3)	15 (12.1)	37 (7.4)
Stroke	38 (6.1)	9 (7.3)	29 (5.8)
Restless legs syndrome	32 (5.1)	8 (6.5)	24 (4.8)
Chronic heart failure	29 (4.6)	7 (5.6)	22 (4.4)
Gastro-oesophageal reflux	22 (3.5)	5 (4.0)	17 (3.4)
Depression (BDI-II)			
No depression	252 (40.2)	38 (30.6)	214 (42.5)
Minimal depression	97 (15.5)	18 (14.5)	79 (15.7)
Mild depression	77 (12.3)	19 (15.3)	58 (11.5)
Moderate depression	73 (11.6)	18 (14.5)	55 (10.9)
Severe depression	27 (4.3)	7 (5.6)	20 (4.0)
Daytime sleepiness (ESS Score)			
0 to 10	358 (57.1)	60 (48.4)	298 (59.2)
11 to 15	163 (26.0)	33 (26.6)	130 (25.8)
16 to 20	59 (9.4)	15 (12.1)	44 (8.7)
21 to 24	5 (0.8)	1 (0.8)	4 (0.8)
SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease; BDI-II: Beck Depression Inventory; ESS: Epworth Sleepiness Scale.			

Table 1: Socio-demographic and clinical characteristics of the study population (n=627).

The three most common medical comorbidities were hypertension (56.9%), diabetes mellitus type 2 (12.0%), and thyroidal diseases (10.5%). The results of the Beck Depression Inventory (BDI-II) indicated that 43.7% of the patients suffered from depressive

symptoms. More female patients were affected by depressive symptoms than male participants.

Daytime sleepiness was evaluated with the Epworth Sleepiness Scale (ESS). A total of 10.2% of the patients were moderately to severely impaired by daytime sleepiness (ESS score 16 to 24 points).

Health-related quality of life

As shown in Figure 1, the majority of the patients were not affected in the domains of self-care and mobility. In contrast, 55.5% and 33.5% of the patients reported moderate or severe problems in the domains of pain/discomfort and anxiety/depression. Usual activities were affected moderately to severely in 29.5% of the sample. Compared with the general population in Germany, patients suffering from OSA were considerably more impaired in all domains of the EQ-5D-3L.

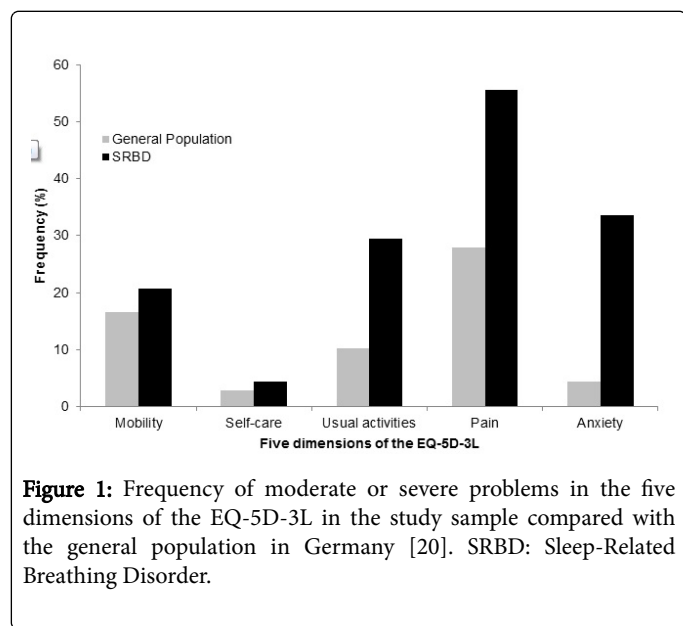


Figure 1: Frequency of moderate or severe problems in the five dimensions of the EQ-5D-3L in the study sample compared with the general population in Germany [20]. SRBD: Sleep-Related Breathing Disorder.

The mean EQ-5D-3L index was 0.86 ± 0.19 and the mean EQ VAS score was 66.8 ± 19.3 . There was a decline in the EQ-5D-3L index and the EQ VAS score with increased patient age ($p=0.016$ and $p=0.028$). As shown in Table 2, male patients reported considerably higher HrQoL than female participants, as well as patients living in a relationship compared with those who were single, divorced or widowed. The EQ VAS score was reduced in patients with no or a lower/intermediate school degree compared with the EQ VAS score of those with better school education ($p=0.013$). The EQ VAS was also reduced in participants without a professional education or with non-academic degrees ($p=0.007$). Limitations in the professional career due to the disease substantially affected patient HrQoL (EQ-5D-3L index: $p=0.007$, EQ VAS: $p=0.002$). Additionally, the EQ-5D-3L index and the EQ VAS score were reduced in patients suffering from medical comorbidities such as hypertension, diabetes mellitus type 2, cardiac arrhythmias, pulmonary and musculoskeletal diseases or chronic obstructive pulmonary diseases. A diminished HrQoL was shown for patients with depressive symptoms ($p<0.001$ for both scores). The EQ-5D-3L index was 0.95 ± 0.10 in patients without depression and was 0.50 ± 0.32 in patients with severe depression. The EQ VAS score was 76.4 ± 15.4 for patients without depressive symptoms and was 45.5 ± 20.6 for severely depressed persons. Furthermore, a considerable association between diminished HrQoL and daytime sleepiness (evaluated with the Epworth Sleepiness Scale) was shown (EQ-5D-3L index and EQ VAS, $p<0.001$): the EQ VAS score was substantially decreased from 70.2 ± 18.0 (ESS score 0 to 10 points) to 48.0 ± 23.6 (ESS score 21 to 24 points) (Table 2).

	EQ-5D-3L index		EQ VAS	
	mean \pm SD	p	mean \pm SD	P
Overall Score	0.86 ± 0.19		66.8 ± 19.3	
Gender		$p=0.001$		$p<0.001$
Female	0.83 ± 0.20		61.4 ± 19.4	
Male	0.87 ± 0.19		68.1 ± 19.1	
Family status		$p=0.025$		$p=0.018$
Living in a relationship	0.87 ± 0.18		67.8 ± 18.7	
Not living in a relationship	0.69 ± 0.34		53.4 ± 27.6	
School Education		$p=0.131$		$p=0.013$
No degree	0.96 ± 0.08		58.3 ± 23.2	
Lower/intermediate degree	0.82 ± 0.24		62.9 ± 21.1	
Higher degree	0.89 ± 0.14		70.9 ± 17.6	
Professional education		$p=0.063$		$p=0.007$
None	0.74 ± 0.30		58.5 ± 24.2	
Academic degree	0.88 ± 0.18		69.6 ± 18.0	
Non-academic degree	0.86 ± 0.19		65.7 ± 19.0	

Professional Career		p=0.007		p=0.002
Limitations due to the disease	0.78 ± 0.25		50.0 ± 24.0	
No limitations	0.88 ± 0.18		68.4 ± 18.8	
Gross income (per month)		p=0.042		p=0.108
Less than 1700 Euros	0.84 ± 0.23		66.1 ± 18.2	
More than 1700 Euros	0.90 ± 0.16		69.8 ± 17.2	
Health insurance		p<0.001		p=0.001
Statutory	0.86 ± 0.20		65.8 ± 19.6	
Private	0.91 ± 0.16		73.6 ± 15.7	
Comorbidities				
Hypertension	0.85 ± 0.21	p=0.001	64.6 ± 19.7	p=0.001
No	0.89 ± 0.18		70.1 ± 19.0	
Diabetes mellitus type 2	0.81 ± 0.25	p=0.018	59.5 ± 21.9	p=0.001
No	0.87 ± 0.18		68.1 ± 18.8	
Cardiac arrhythmia	0.84 ± 0.18	p=0.029	60.8 ± 18.8	p=0.005
No	0.87 ± 0.19		68.1 ± 19.1	
Pulmonary diseases	0.82 ± 0.23	p=0.056	62.8 ± 18.6	p=0.045
No	0.87 ± 0.19		67.9 ± 19.5	
Musculoskeletal diseases	0.77 ± 0.25	p=0.002	57.1 ± 21.5	p<0.001
No	0.88 ± 0.18		68.0 ± 19.0	
COPD	0.77 ± 0.27	p=0.005	53.4 ± 20.2	p<0.001
No	0.87 ± 0.19		68.8 ± 18.8	
Depression (BDI-II)		p<0.001		p<0.001
No depression	0.95 ± 0.10		76.4 ± 15.4	
Minimal depression	0.90 ± 0.13		66.2 ± 16.5	
Mild depression	0.79 ± 0.19		57.1 ± 18.0	
Moderate depression	0.72 ± 0.24		54.0 ± 15.8	
Severe depression	0.50 ± 0.32		45.5 ± 20.6	
Daytime sleepiness (ESS Score)		p<0.001		p<0.001
0 to 10	0.89 ± 0.17		70.2 ± 18.0	
11 to 15	0.83 ± 0.22		62.0 ± 19.7	
16 to 20	0.82 ± 0.22		59.3 ± 18.3	
21 to 24	0.89 ± 0.04		48.0 ± 23.6	
SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease; BDI-II: Beck Depression Inventory; ESS: Epworth Sleepiness Scale				

Table 2: Bivariate associations between the EQ-5D-3L index and the EQ VAS score and socio-demographic data and clinical subscales.

Finally, patient age, gender, family status, school education, the presence of medical comorbidities, daytime sleepiness and the occurrence of depressive symptoms were included in the multivariate regression models. As shown in Table 3, the presence of depression as

well as further medical comorbidities was considerably associated with lower EQ-5D-3L and EQ VAS values. Additionally, the results of the EQ VAS were significantly correlated with increasing age and daytime

sleepiness. Multivariate regression analyses were able to explain approximately 35.9% (dependent variable: EQ-5D-3L index, model 1) and 34.9% (dependent variable: EQ VAS, model 2) of the variance.

	Model 1				Model 2			
	EQ-5D-3L index				EQ VAS			
	B	Bootstrap Std. Error	Lower bound	Upper bound	B	Bootstrap Std. Error	Lower bound	Upper bound
Age (years)	-0.001	0.001	-0.002	0.001	-0.144*	0.066	-0.273	-0.014
Gender	-0.001	0.021	-0.039	0.035	2.364	2.131	-2.027	6.518
Family Status	-0.022	0.013	-0.048	0.005	-1.517	1.262	-4.058	1.035
School Education	-0.004	0.01	-0.024	0.016	-0.306	1.006	-2.219	1.589
Presence of Comorbidities	-0.041*	0.019	-0.08	0	-6.726*	1.618	-9.869	-3.491
Daytime Sleepiness (ESS Score)	0.001	0.002	-0.003	0.005	-0.607*	0.212	-1.019	-0.197
Depression (BDI-II Score)	-0.013*	0.002	-0.016	-0.01	-1.013*	0.095	-1.198	-0.824
Constant	1.089	0.069	0.948	1.229	95.291	5.848	83.911	106.283

ESS: Epworth Sleepiness Scale; BDI-II: Beck Depression Inventory; B: Regression Coefficient; *Significant at p<0.05

Table 3: Multivariate linear regression analyses to evaluate the association between selected socio-demographic and clinical factors with patients' HrQoL.

Discussion

The male/female ratio in this cohort showed a male preponderance as expected and as shown in large international studies [21]. Women are known to develop sleep apnea substantially later than men. Moreover, OSA is likely underdiagnosed in women. Only 36% of the patients reported daytime sleepiness as measured by the ESS. In the majority of patients, the ESS was between 0-10 points. This finding is typical for OSA patients. Many patients are not aware of their sleepiness despite falling asleep or dozing off in public. A large prospective review found that 21.8% of patients with OSA had a higher prevalence of depression than patients without OSA (9.4%) [22]. A longitudinal study in Taiwanese OSA patients by Chen et al. showed a 2.18-fold higher risk to develop depression within one year after the diagnosis for patients with OSA compared with that of the controls [23]. Further clinical investigations found a prevalence of depression in approximately 5%-63% of patients with OSA [24]. This wide range may be the result of confounders due to co-morbid disorders and the insufficient separation of the sequelae of depression and OSA.

The mean EQ VAS of patients in this study was 66.8 ± 19.3 and was similar to that of patients with narcolepsy as measured in a cohort of 75 patients with narcolepsy by Dodel et al. (mean EQ VAS: 60.7) [25]. This result is surprising because OSA is a disorder that has an excellent treatment outcome. Several previous studies evaluated the association between HrQoL in OSA patients and depression, as well as excessive daytime sleepiness (EDS). In general, an increase in depressive symptoms and excessive daytime sleepiness was associated with poorer HrQoL [10]. Thus, our results are in line with the majority of international evaluations. A cross-sectional study by Lee et al. evaluated the contributions of depression (Beck Depression

Inventory), daytime sleepiness (Epworth Sleepiness Scale), apnea severity, and sleep quality to HrQoL in 793 incident and untreated OSA patients, as measured using the SF-36. It was found that 46.2% of the study sample suffered from depression [26]. The extent of depressive symptoms was the strongest variable influencing the physical and mental domains of HrQoL. However, excessive daytime sleepiness affected only the physical aspects of HrQoL. Silva et al. also used the SF-36 to prospectively assess HrQoL among 3,708 patients with sleep-related breathing disorders over five years. The authors reported a significant association between excessive daytime sleepiness and poorer HrQoL [6]. Akashiba et al. included 60 patients with severe OSA to evaluate the influence of depressive mood, excessive daytime sleepiness and polysomnographic parameters on HrQoL (SF-36) compared with healthy controls, resulting in lower HrQoL in OSA patients [10]. Furthermore, depression and excessive daytime sleepiness were the most important predictors of HrQoL in multivariate regression analysis.

The results of our study should be interpreted in the context of several limitations. Our study included 627 patients, which is a relatively small sample size compared with earlier evaluations [6,26]. Additionally, the study was conducted in a regional design, and the patients were consecutively recruited. Therefore, the study sample may not be representative of all German patients suffering from OSA or patients outside of Germany. To our knowledge, this is the first study evaluating HrQoL in patients with OSA in Germany that uses patients from specialized health care settings (sleep laboratories) in a regional study design. In conclusion, depressive disorders, excessive daytime sleepiness and the presence of medical comorbidities had a significant

effect on patient HrQoL and should be considered in the treatment of OSA patients to improve the HrQoL of those patients.

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Conflicts of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual patients included in the study.

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