



OSA and CPAP therapy: effect of gender, somnolence, and treatment adherence on health-related quality of life

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Abstract

Background Obstructive sleep apnea (OSA) often has a significant impact on health-related quality of life (HRQoL) with social and psychological implications. For most OSA patients, a reduction in their HRQoL is due to symptoms such as poor sleep quality, excessive daytime somnolence, and fatigue with differences between gender.

Purpose This study explores the CPAP treatment effect on self-perceived HRQoL related to gender, somnolence, and CPAP adherence.

Methods Out of 1082 consecutive Italian outpatients, 125 (82 M) (60.3 ± 9.6 years) completed the prospective observational study and were evaluated at the first visit (T0), and the follow-up visit (T1). Two self-reported HRQoL questionnaires were administered: six subscales Psychological General Well-Being Index (PGWBI) and 12-Item Short-Form Health Survey (SF-12).

Results Scores of PGWBI and SF-12 MCS improved from T0 to T1. Patients with CPAP use ≥ 4 h/night showed a significant improvement in all dimensions evaluated, except for SF-12 PCS. At T1, participants with ESS > 10 improved in all scores, except SF-12 PCS. Gender comparison shows better-perceived HRQoL in males at first visit and CPAP follow-up visit. Variation of PGWBI was significantly correlated with CPAP use, ESS at T0 and T1 ($p < 0.0001$; $r^2 = 0.26$).

Conclusions This study provides evidence on the effectiveness of CPAP treatment on perceived HRQoL. Participants with greater adherence to therapy, greater sleepiness, and greater improvement of daytime sleepiness with CPAP therapy, reported a higher quality of life improvement. Gender comparison shows better-perceived HRQoL in males at first visit and CPAP follow-up, despite a more considerable improvement in females.

Keywords CPAP adherence · Excessive daytime sleepiness · Gender · Quality of life · Obstructive sleep apnea

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Background

Obstructive sleep apnea (OSA) is a treatable disordered breathing characterized by repetitive narrowing or obstruction of the upper airway during sleep, apneas or hypopneas, associated with sleep disruption, progressively increasing respiratory efforts, intermittent hypoxia, systemic and pulmonary arterial blood pressure fluctuations. Up to 9% of women and 24% of men in the general middle age population have at least an apnea-hypopnea index (AHI) of five per hour [1].

Obstructive sleep apnea patients may exhibit a significant impact on health-related quality of life (HRQoL), including its social and psychological domains with gender differences [2].

There are different options for OSA treatment like lifestyle recommendations, mandibular advancement devices, surgical procedures, etc. However, continuous positive airway pressure (CPAP) is the most effective and commonly used treatment for moderate-severe OSA or mild OSA with

comorbidities [3]. It is well established that CPAP use improves sleep quality, oxygen saturation, daytime sleepiness, blood pressure, cardiovascular risk, and enhances HRQoL [4] with a CPAP use time relationship [5]. Unfortunately, many patients do not use CPAP enough to improve daytime performance [6]. Health-related quality of life is one of the significant patient-reported outcomes in healthcare. For most OSA patients, a reduction in their HRQoL is due to symptoms such as EDS, fatigue, poor sleep quality, and trouble sharing the bedroom with the bed partner. These are the primary reasons for pursuing care. Somnolence perception, when present, plays a significant role in determining deterioration of HRQoL [7–14]. In the Sleep Heart Health Study, one-third of severe OSA patients had EDS [13], and effective OSA treatment, with EDS reduction, should result in an improvement of the patients HRQoL [15].

Women with OSA have significantly lower HRQoL than men [10]. Studies are increasingly designed to understand gender differences in the OSA clinical features better. Women with OSA report significantly lower functional status, variable subjective daytime sleepiness, poorer neurobehavioral performance, and more fatigue and mood disturbance compared to men at baseline [16, 17]. Studies on CPAP adherence and gender provided conflicting results: females were found to have a lower as well as an increased CPAP adherence [11, 16]. Lack of consistency in findings may be due to the differences between the sample characteristics, such as age and symptoms severity.

Nevertheless, the impact of CPAP treatment on many aspects related to perceived HRQoL, like mood, psychological well-being, self-control, fatigue, and mental and physical health, need further investigation.

This paper explores the relationship between gender, somnolence, and CPAP adherence on HRQoL. We analyzed the HRQoL in OSA patients at first visit and after CPAP treatment.

Methods

The study involved Italian patients attending our Sleep Center for respiratory disorders during sleep. Out of 1082 consecutive outpatients in a time interval between mid-2015 and mid-2016, 125 participants completed the prospective observational study (43 F, 82 M); age 32–82 years (60.3 ± 9.6). CPAP-naïve patients with OSA diagnosis and CPAP prescription and with at least primary education were eligible to be included in the study. Patients with a previous diagnosis or on treatment for OSA (n. 263) as well as patients affected by psychiatric or neurological disease and participants taking neurological medication (n. 7) were not included in the analysis. Subjects who did not complete the full diagnostic process, CPAP titration, follow-up or questionnaires (n. 493), and negative for OSA or eligible for alternative treatment or refused CPAP

(n. 194) were excluded from the study (Fig. 1). The age, gender, and BMI of all eligible patients for the study were analyzed. No significant differences were found between patients who participated in the study and those excluded.

All of the participants went through clinical evaluation, including sleep-related disorders. The study received Institutional Ethical Committee approval (Palermo I AOUP “P. Giaccone,” report number 8/2014) and all participants gave written informed consent for personal data processing.

A portable computerized system (type III) was employed to perform nocturnal monitoring, (Somté or Somnea Compumedics Inc.; Abbotsford, VIC, Australia). A sleep technician performed the setup. The following signals were recorded: airflow by nasal cannula pressure, snoring, thoracic and abdominal movements, body position, limb movements, arterial oxygen saturation, pulse rate, and pulse waveform. Recordings duration were at least 6 h. According to standard criteria of the American Academy of Sleep Medicine, apneas and hypopneas were visually scored, and OSA severity was defined [18]. Percent study-time with O_2 saturation $< 90\%$ (TSat90) was evaluated.

Questionnaires

The *psychological general well-being (PGWB)* was administered for exploration of subjective well-being of participants as

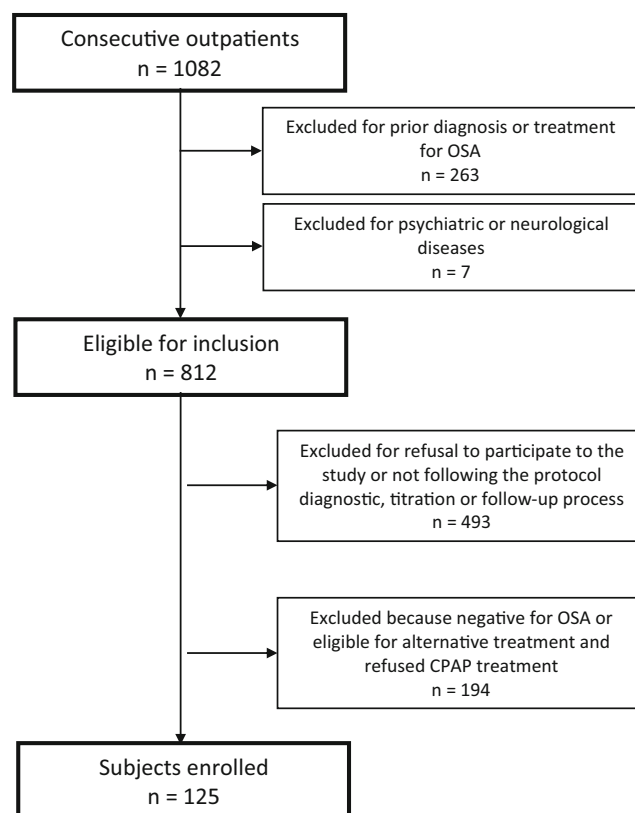


Fig. 1 Consort flow chart: participants to the study enrolled for the HRQoL evaluation at first visit and follow-up

previously described (7–9). It is a 22-item questionnaire consisting of six subscales: Anxiety, Depression, Well-being, Self-control, Health, and Vitality. Item responses are rated on a six-point Likert scale ranging from 0 to 5. The subscales sum provides a global index score for subjective well-being (range 0–110) with higher scores indicating better well-being. Considering “distress” as the opposite of well-being, a global score < 60 suggests a “Severe Distress”; from 60 to 72 a “Moderate Distress”; and > 72 “No Distress” category [19, 20].

The 12-Item Short-Form Health Survey (SF-12) was administered to measure both Physical (PCS) and Mental health. The Physical (PCS) and Mental Component Summary (MCS) are standardized (range 0–100) with a reference value of 50: a score above 50 means better than average function while below 50 means poorer than average function [21, 22].

The Italian version of the Epworth Sleepiness Scale (ESS) [23, 24] was administered to assess daytime sleepiness. A score above 10 suggests EDS.

Study procedure

Patients' HRQoL was assessed at the first visit (T0), and the first follow-up (T1) from a minimum of 2 to a maximum of 9 months of CPAP therapy. The study did not affect either the patients' diagnostic procedure and routine care or the timing of CPAP follow-up. After the diagnosis of OSA, the relevance of adherence to CPAP and the consequences of failed treatment were illustrated. Subsequently, after identification of the mask and an educational and training session, patients underwent CPAP titration with an auto-adjusting device (S9TM, ResMed Ltd., Bella Vista, Australia) for 3 to 5 nights at the patients' home or in the sleep lab. After a critical revision of recordings, the level of pressure only rarely exceeded, was selected as the CPAP treatment level [25]. CPAP adherence was assessed by monitoring CPAP use per night by CPAP software program at the scheduled first follow-up visit. The adherence criterion used is at least 4 h per night. An assistant psychologist administered questionnaires at T0 and T1 in the same order: ESS, followed by PGWBI and SF-12.

Statistical analysis

Data are reported as mean \pm SD. The relationship between gender, age, BMI, AHI, TSat90, adherence (hours of CPAP therapy/night), ESS at T0 and T1 and changes in PGWBI was analyzed using multiple linear regression. Continuous variables were tested for normality of distribution by the Kolmogorov-Smirnov test. Non-parametric Wilcoxon's test and non-parametric pairwise multiple comparison Wilcoxon's test were used to assess differences. The questionnaires mean differences between T0 and T1 were evaluated by paired *t* test. Cohen's *d* effect size, for the two paired samples (T0, T1), was estimated dividing the *t* value of the paired *t* test

by the square root of the number of pairs. Effect size shows the magnitude of differences observed [26]. Pearson's chi-square was applied to assess differences in “Distress category” between T0 and T1. $p < 0.05$ was considered significant. Statistical analysis was performed by commercial software (JMP 8.0 SAS Institute Inc.).

Results

Population characteristics and nocturnal sleep study results at T0, and CPAP adherence are shown in Table 1. The population was divided by gender, drowsiness (ESS score ≤ 10 and ESS score > 10 at T0) and CPAP adherence (use $<$ and ≥ 4 h/night). Comparisons did not show any statistical difference in the parameters. There were no statistically significant differences for age, BMI, AHI, TSat90, adherence, and ESS between females and males, somnolent and no-somnolent, and adherent and no-adherent participants.

Table 2 shows PGWBI, SF-12, and ESS scores at T0 and T1. Mean scores at T0 were worse than reference values in the whole sample [18, 20, 22] ($p < 0.0147$). The PGWBI scores improved at T1 compared to T0; the PGWBI total score and the Anxiety, Depression, Well-Being, and Vitality score of the subscales became similar to reference values. The SF-12 showed an improvement for the MCS, but not for the PCS. A medium level of effect size for PGWBI total score and Vitality subscale score was observed. ESS mean score decreased by a significant amount from T0 to T1 (11.2 to 5.1 respectively). Multiple linear regression analysis was applied between changes in PGWBI and gender, age, BMI, AHI, TSat90, adherence (hours of CPAP therapy/night), and ESS at T0 and T1. PGWBI variation was significantly correlated with adherence to therapy, ESS at T0 and T1 ($p < 0.0001$; $r^2 = 0.26$). Greater adherence to therapy, greater sleepiness at T0, and a greater reduction in daytime sleepiness at T1 were associated with improved quality of life.

Distress category distribution was different between T0 and T1 ($r^2 = 0.16$ - chi-square = 55.387; $p < 0.0001$), with an increase, after CPAP therapy, of participants with a total score > 72 (no-distress).

Table 3 shows PGWBI, SF-12, and ESS scores for each gender. Males compared to females showed higher mean scores at both times ($p < 0.0022$), except for ESS. At T1 females improved all scores unless the Self-control PGWBI subscale and the SF-12 PCS with a large effect size in the ESS and a medium effect size improvement in the PGWBI total score and the Well-Being and the Vitality subscales. Males showed a large effect size in ESS and medium effect size on Vitality PGWBI subscale. After CPAP treatment, female improved more subscales than male did; however, their HRQoL scores remained worse.

Table 1 Patients characteristics and nocturnal polygraphic results

	Total	Female	Male	ESS ≤ 10	ESS > 10	CPAP use < 4 h/night	CPAP use ≥ 4 h/night
Participants, no.	125	43	82	56 (13F, 43 M)	69 (30F, 39 M)	22 (6F, 16 M)	103 (37F, 66 M)
Age, years	60.3 ± 9.6	62.7 ± 8.4	59.1 ± 10.0	61.1 ± 9.7	59.7 ± 9.5	61.2 ± 9.8	60.1 ± 9.6
BMI, kg/m ²	33.5 ± 6.6	35.1 ± 7.9	32.6 ± 5.6	32.2 ± 5.3	34.5 ± 7.3	30.9 ± 3.9	34.0 ± 6.9
AHI, n/h	47.5 ± 24.2	44.1 ± 27.0	49.2 ± 22.5	43.5 ± 20.0	50.7 ± 26.8	42.0 ± 25.3	48.6 ± 23.9
Mild, no. (%)	10 (8.0)	4 (9.3)	6 (7.3)	4 (7.2)	6 (8.7)	1 (4.5)	9 (8.8)
Moderate, no. (%)	25 (20.0)	12 (27.9)	13 (15.9)	11 (19.6)	14 (20.3)	9 (41.0)	16 (15.5)
Severe, no. (%)	90 (72.0)	27 (62.8)	63 (76.8)	41 (73.2)	49 (71.0)	12 (54.5)	78 (75.7)
TSat90, %	26.1 ± 24.7	27.9 ± 26.7	25.2 ± 23.6	22.6 ± 24.0	29.0 ± 25.0	19.9 ± 24.2	27.4 ± 24.7
Adherence, h/night	5.4 ± 1.7	5.5 ± 1.8	5.3 ± 1.7	5.2 ± 1.9	5.5 ± 1.6	–	–
ESS score at T0	11.2 ± 5.1	12.0 ± 5.0	10.8 ± 5.2	–	–	9.5 ± 5.6	11.6 ± 5.0

BMI, body mass index; *AHI*, apnea-hypopnea index; Mild = $5 \leq \text{AHI} < 15$; Moderate = $15 \leq \text{AHI} < 30$; Severe = $\text{AHI} \geq 30$ per hour; *TSat₉₀* = percent study-time at less than 90% oxygen saturation; *ESS*, Epworth Sleepiness Scale; Time of first visit; *CPAP*, continuous positive airway pressure; *F*, female; *M*, Male. Data are expressed as mean ± SD, unless otherwise indicated. There were no statistically significant differences for age, BMI, AHI, Tsat90, adherence, and ESS between the groups: female and male; ESS ≤ 10 and > 10; CPAP use < 4 h/night and CPAP use ≥ 4 h/night

In Table 4, the sample is divided by ESS score ≤ 10 and ESS score > 10 at first visit and follow-up. Comparison of PGWBI and SF-12 scores at T0 showed higher scores in both questionnaires ($p < 0.0421$) for ESS ≤ 10 group unless the Anxiety PGWBI subscale. At T1, there were no differences in HRQoL scores between ESS score groups. At T1 compared to T0, the group with ESS ≤ 10 improved only in the Vitality PGWBI subscale ($p = 0.0031$), with a medium effect size related to sleepiness improvement. The group with ESS > 10 improved in all scores except one (SF-12 PCS), with a large effect size on PGWBI total score and Vitality subscale, and a medium effect size on Depression, Well-Being, and Health PGWBI subscales. Sleepiness improved in both groups; however, this was more evident after CPAP therapy in the ESS >

10 group. Namely, participants with EDS at first visit improved in more subscales with a larger effect size than those with ESS ≤ 10.

Table 5 shows the sample divided by CPAP use < or ≥ 4 h/night. The comparison among PGWBI, SF-12, and ESS scores at T0 indicates that HRQoL and ESS were not different. At T1 the group with CPAP use ≥ 4 h/night had an improvement in almost all HRQoL dimensions; we found statistically significant differences between groups for PGWBI total score ($p = 0.0125$), Depression ($p = 0.0072$), Well-being ($p = 0.0051$) and Vitality ($p = 0.0281$) PGWBI subscales, and SF-12 MCS ($p = 0.0127$). At T1, the group with a CPAP use < 4 h/night improved only in ESS, while the “adherent” group (CPAP use ≥ 4 h/night), improved in most scores except SF-12 PCS, and effect size indicated substantial change in ESS and Vitality PGWBI subscale and a medium improvement in PGWBI total score and Well-being subscale.

Table 2 Health-related quality of life and ESS before and after CPAP therapy

	T0	T1	Effect Size
PGWBI	69.0 ± 17.4	77.5 ± 17.2*	0.53
Anxiety	15.7 ± 5.0	17.6 ± 4.6*	0.36
Depression	11.8 ± 2.7	12.5 ± 2.4**	0.26
Well-being	10.8 ± 4.1	12.3 ± 4.0*	0.38
Self-control	10.4 ± 3.2	11.1 ± 2.9 [†]	0.24
Health	9.3 ± 2.8	10.3 ± 2.7*	0.37
Vitality	10.9 ± 3.8	13.9 ± 3.5*	0.77
SF-12 PCS	43.0 ± 9.8	44.1 ± 10.7	–
SF-12 MCS	44.2 ± 10.8	46.9 ± 10.1**	0.26
ESS	11.2 ± 5.1	5.1 ± 4.4*	1.07

PGWBI, Psychological General Well-Being Index; *SF-12*, 12-Item Short-Form Health Survey; *PCS*, Physical Component Summary; *MCS*, Mental Component Summary; *ESS*, Epworth Sleepiness Scale; *T0*, time of first visit; *T1*, time of follow-up visit; Data are given as mean ± SD

Comparison of T0 vs T1: * $p < 0.0001$, ** $p < 0.005$, [†] $p < 0.05$

Discussion

This study provides a better understanding of gender, excessive daytime somnolence, and CPAP adherence, on HRQoL. Gender comparison showed higher HRQoL scores in males at first visit and follow-up, despite a more considerable improvement with CPAP in females. At T1, the PGWBI scores improved. At first visit, participants with EDS had a worse HRQoL than those without, irrespective of OSA severity. At follow-up, the EDS group improved their perceived well-being achieving values similar to the non-EDS group that had a satisfactory HRQoL level on the first visit. Participants with a CPAP adherence of at least 4 h/night improved almost all HRQoL questionnaires scores.

Table 3 Health-related quality of life and ESS by gender before and after CPAP therapy

	Female (43)			Male (82)		
	T0	T1	Effect Size	T0	T1	Effect Size
PGWBI	57.5 ± 16.9	69.4 ± 15.5*	0.68	75.0 ± 14.5	81.8 ± 16.6*	0.46
Anxiety	13.2 ± 5.0	16.0 ± 4.1**	0.47	16.9 ± 4.5	18.3 ± 4.7†	0.30
Depression	10.4 ± 3.0	11.7 ± 2.1**	0.51	12.5 ± 2.2	12.9 ± 2.5	–
Well-being	8.2 ± 3.3	10.5 ± 3.8**	0.58	12.2 ± 3.8	13.2 ± 3.9†	0.28
Self-control	8.7 ± 3.4	9.6 ± 2.7	–	11.3 ± 2.6	11.8 ± 2.8	–
Health	7.8 ± 2.8	9.1 ± 2.7†	0.43	10.1 ± 2.5	10.9 ± 2.5**	0.34
Vitality	9.1 ± 3.7	12.4 ± 3.5*	0.79	11.8 ± 3.5	14.6 ± 3.2*	0.76
SF-12 PCS	37.8 ± 9.2	39.9 ± 10.8	–	45.8 ± 9.0	46.4 ± 9.9	–
SF-12 MCS	37.7 ± 9.2	42.9 ± 10.5**	0.46	47.6 ± 10.0	49.0 ± 9.3	–
ESS	12.0 ± 5.0	6.0 ± 5.1*	1.0	10.8 ± 5.2	4.6 ± 3.9*	1.1

PGWBI, Psychological General Well-Being Index; SF-12, 12-Item Short-Form Health Survey; PCS, Physical Component Summary; MCS, Mental Component Summary; ESS, Epworth Sleepiness Scale; T0, time of first visit; T1, time of follow-up visit; Data are given as mean ± SD

Comparison of T0 vs T1: * $p < 0.0001$, ** $p < 0.005$, † $p < 0.05$

OSA symptoms are significantly different between genders. Women with OSA have more comorbidities and have a higher level of health care utilization compared to men [11, 12]. Women with OSA report significantly lower functional status, variable subjective daytime sleepiness, higher frequency of apnea symptoms, more mood disturbance, and poorer neurobehavioral performance than men at baseline [16, 17]. A possible explanation includes the hypothesis that OSA women may refer their sleepiness differently, and emphasize lack of energy, fatigue, or tiredness more than sleepiness. Independently of age and AHI, depression and anxiety have been reported to be higher in women [11, 27]. Lower values of females HRQoL could be explained by more significant

attention to body care, as well as a social habit for females to express distress rather than report poorer well-being and higher symptom complaint rate [28]. Previous studies suggest a poorer HRQoL and more psychological morbidity in OSA females than OSA males, perhaps due to the different ways of experiencing the disease [10, 11].

Nevertheless, both genders improved their HRQoL with CPAP treatment. Sforza et al. [29] showed a relationship between the severity of the psychological symptoms in OSA subjects and daytime sleepiness. Jacobsen et al. [14] showed that EDS in OSA patients was the most tightly related to emotional functioning and interpersonal relationship, although it may not be their only determinant. Kang et al. [30]

Table 4 Health-related quality of life and ESS by somnolence before and after CPAP therapy

	ESS ≤ 10 (56; 13 F, 43 M)			ESS > 10 (69; 30 F, 39 M)		
	T0	T1	Effect Size	T0	T1	Effect Size
PGWBI	74.6 ± 15.2	77.1 ± 18.7	–	64.4 ± 17.8	77.9 ± 16.1*	0.83
Anxiety	16.2 ± 4.6	17.3 ± 5.1	–	15.2 ± 5.2	17.8 ± 4.3**	0.45
Depression	12.5 ± 2.2	12.2 ± 2.8	–	11.2 ± 3.0	12.8 ± 2.0*	0.65
Well-being	11.8 ± 3.7	12.0 ± 4.1	–	10.0 ± 4.2	12.5 ± 4.0*	0.63
Self-control	11.3 ± 2.7	11.2 ± 3.2	–	9.6 ± 3.3	10.9 ± 2.7**	0.48
Health	10.0 ± 2.6	10.5 ± 2.7	–	8.8 ± 2.8	10.1 ± 2.7*	0.50
Vitality	12.6 ± 3.4	13.9 ± 3.5**	0.41	9.5 ± 3.5	13.8 ± 3.5*	1.12
SF-12 PCS	45.1 ± 8.4	45.8 ± 10.5	–	41.3 ± 10.6	42.8 ± 10.7	–
SF-12 MCS	47.0 ± 10.3	46.7 ± 10.0	–	41.9 ± 10.7	47.0 ± 10.3**	0.47
ESS	6.7 ± 2.7	4.1 ± 4.0*	0.60	14.9 ± 3.3	5.9 ± 4.6*	1.78

PGWBI, Psychological General Well-Being Index; SF-12, 12-Item Short-Form Health Survey; PCS, Physical Component Summary; MCS, Mental Component Summary; ESS, Epworth Sleepiness Score; T0, time of first visit; T1, time of follow-up visit; F, female; M, male. Data are given as mean ± SD. Comparison of T0 vs T1: * $p < 0.0001$, ** $p < 0.005$

Table 5 Health-related quality of life and ESS by CPAP adherence before and after CPAP therapy

	CPAP use < 4 h/night, <i>n</i> = 22 (6 F; 16 M)			CPAP use ≥ 4 h/night, <i>n</i> = 103 (37 F; 66 M)		
	T0	T1	Effect Size	T0	T1	Effect Size
PGWBI	71.7 ± 15.4	68.0 ± 19.9	–	68.4 ± 17.8	79.6 ± 16.0*	0.75
Anxiety	16.3 ± 5.1	15.7 ± 5.1	–	15.5 ± 5.0	17.9 ± 4.5*	0.48
Depression	12.1 ± 2.7	11.1 ± 3.2	–	11.7 ± 2.7	12.8 ± 2.1*	0.45
Well-being	11.2 ± 4.1	9.9 ± 4.3	–	10.7 ± 4.1	12.8 ± 3.8*	0.59
Self-control	11.0 ± 2.1	10.0 ± 3.4	–	10.2 ± 3.3	11.3 ± 2.8*	0.39
Health	9.2 ± 2.7	9.2 ± 3.2	–	9.4 ± 2.8	10.5 ± 2.6*	0.48
Vitality	11.9 ± 4.0	12.2 ± 3.9	–	10.7 ± 3.7	14.2 ± 3.3*	0.96
SF-12 PCS	40.3 ± 10.7	40.1 ± 13.1	–	43.6 ± 9.6	45.0 ± 9.9	–
SF-12 MCS	45.2 ± 8.9	42.3 ± 9.8	–	44.0 ± 11.2	47.9 ± 10.0**	0.37
ESS	9.5 ± 5.6	6.3 ± 5.9†	0.49	11.6 ± 5.0	4.9 ± 4.0*	1.26

PGWBI, Psychological General Well-Being Index; SF-12, 12-Item Short-Form Health Survey; PCS, Physical Component Summary; MCS, Mental Component Summary; ESS, Epworth Sleepiness Scale; T0, time of first visit; T1, time of follow-up visit; CPAP, continuous positive airway pressure; F, female; M, male. Data are given as mean ± SD. Comparison of T0 vs T1: * $p < 0.0001$, ** $p < 0.005$, † $p < 0.05$

showed that the most critical factor affecting HRQoL of OSA subjects is their subjective perception of sleep quality rather than the AHI.

Similarly, Billings et al. [31] underscored the persistent weak link between objective measures of physiological disturbances and the subjective patient-reported outcomes. While OSA severity was not related to the level of HRQoL and not sufficient to understand implications for treatment [32], EDS affects many aspects of life, so that sleepy people feel more limited by their health conditions. Our data show that the HRQoL perception got worse with greater sleepiness, pointing out how EDS affects negatively all HRQoL dimensions we analyzed. In our sample, the gender differences in HRQoL were not affected by perceived EDS; in fact, there were no differences in ESS scores between males and females. Baldwin et al. [33] found that women reported fatigue more frequently than men, although they do not often report drowsiness (ESS > 10). The different perception of drowsiness between males and females may explain the more significant impact of OSA on HRQoL in the latter [34]. Anyway, the EDS group had an improvement in almost all of the HRQoL dimensions with CPAP treatment.

Weaver et al. [35] pointed out that more CPAP use determines a greater reduction of drowsiness, and previous studies have shown the same behavior with CPAP adherence using different HRQoL scales [31, 36]. More CPAP use appears to be associated with both objective and subjective sleep quality and daytime sleepiness improvements [37]. Subjective judgments of improvements in symptoms and daily physical and mental health with CPAP therapy may balance the costs of using it [35]. The expectation of improved HRQoL may motivate patients to undergo testing and treatment for sleep apnea [38]. CPAP treatment of OSA can require considerable changes in a patient's lifestyle: careful thought and follow-up are

required [39]. Our results show that patients with a CPAP use > 4 h/night improved in almost all HRQoL scores, while a CPAP use < 4 h/night did not improve HRQoL, showing how proper CPAP use is required to improve the HRQoL. The effectiveness of CPAP on somnolence, fatigue, irritability, impaired memory, and concentration partly explained HRQoL improvement [4]. Quality of life is worse in untreated OSA patients, independently of severity, when compared with the general population. [40]. Other studies have analyzed the effect of CPAP therapy on HRQoL, underlining a significant improvement of domains such as vitality, social functioning, mental health, and daily functioning or depressive symptoms [41].

Our study shows that the improvement in perceived HRQoL is noticeable in any dimension analyzed, except for SF-12 PCS. In previous studies, we observed the same lack of improvements in this dimension hypothesizing that after a substantial period of therapy, also this dimension would be significantly improved [8, 9]. Now, it is possible to assume that the domains analyzed for SF-12 PCS are not sensitive in detecting health perception changes in OSA patients, looking at not specific dimensions of this condition such as bodily pain.

We found no difference in CPAP adherence between genders. The absence of relationship observed between gender and CPAP adherence might be due to different representativeness in the analyzed population. Some studies examining gender differences in CPAP adherence have produced conflicting results [11]. Gender was not an independent predictor of long-term CPAP use. Long-term CPAP use was positively associated with improvement of subjective daytime sleepiness [30]. The effects of OSA on HRQoL are multifactorial, including psychosocial and psychological factors, all involved in physical and mental health perception.

A limitation of the study concerns the different size of groups after the split for CPAP adherence, with few patients in the group with a CPAP use < 4 h/night. Furthermore, SF-36 could have potentially provided better discrimination than SF-12. However, to obtain a further extension of HRQoL, PGWBI and SF-12 were administered together, avoiding too many items during the administration. The study, despite these limitations, HRQoL.

Conclusion

In summary, this study provides evidence on the effectiveness of CPAP treatment on perceived HRQoL. Participants with greater adherence to therapy, greater sleepiness, and greater improvement of daytime sleepiness with CPAP therapy, reported a higher quality of life improvement. Gender comparison shows better-perceived HRQoL in males at first visit and CPAP follow-up, despite a more considerable improvement in females. Subjects with perceived somnolence, report a worse perceived HRQoL than subjects without EDS, but after CPAP treatment, HRQoL scores of both groups were similar.

Furthermore, our results confirm that a CPAP use ≥ 4 h/night provides a more significant improvement in general HRQoL and most specific dimensions analyzed (mood, anxiety, psychological well-being, self-control, mental and physical health, energy, EDS). Our data indicate the usefulness of investigating patients HRQoL in order to monitor the effect of CPAP therapy and evaluate its individualized effectiveness in enhancing perceived well-being. Appropriately sized samples are essential to fully elucidate the role of gender on HRQoL after CPAP therapy.

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Availability of data and material All data generated or analyzed during this study are included in this published article. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication All participants gave written informed consent for personal data processing.

Authors' contributions LBA contributed to design the study, contributed to the interpretation of the data and drafted the manuscript. SA conceived the study, was responsible for the collection of data and their organization in a database and drafted the manuscript. IIS collected baseline data contributed to the organization in a database. RS performed the statistical analysis, contributed to the interpretation of the data and critical revision of the article. IG conceived the study, collected baseline data, contributed to the interpretation of the data and performed a critical revision of the article. All Authors actively discussed the subject, revised the paper, and provided final approval.

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Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

Ethics approval and consent to participate The Ethical Committee "Palermo I AOUP "P. Giaccone" (report number 8/2014) approved the study.

Abbreviations AHI, apnea-hypopnea index; BMI, body mass index; CPAP, continuous positive airway Pressure; EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; HRQoL, health-related quality of life; MCS, SF-12 Mental Component Summary; OSA, obstructive sleep apnea; PCS, SF-12 Physical Component Summary; PGWBI, Psychological General Well-Being Index; SF-12, 12-Item Short-Form Health Survey; T0, time of first visit; T1, time of first follow-up visit; TSat90, percent study-time at less than 90% oxygen saturation

References

1. Young T, Peppard PE, Gottlieb DJ (2002) Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 165:1217–1239
2. Lee W, Lee SA, Ryu HU, Chung YS, Kim WS (2016) Quality of life in patients with obstructive sleep apnea: relationship with daytime sleepiness, sleep quality, depression, and apnea severity. *Chron Respir Dis* 13:33–39
3. Epstein LJ, Kristo D, Strollo PJ Jr et al (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 5:263–726
4. Diamanti C, Manali E, Ginieri-Coccosis M, Vougas K, Cholidou K, Markozannes E, Bakakos P, Liappas I, Alchanatis M (2013) Depression, physical activity, energy consumption, and quality of life in OSA patients before and after CPAP treatment. *Sleep Breath* 17:1159–1168
5. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE (2011) A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Med Rev* 15:343–356
6. Luyster FS, Dunbar-Jacob J, Aloia MS, Martire LM, Buysse DJ, Strollo PJ (2016) Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behav Sleep Med* 14:67–84
7. Iacono Isidoro S, Salvaggio A, Lo Bue A, Romano S, Marrone O, Insalaco G (2013) Quality of life in patients at first time visit for sleep disorders of breathing at a sleep Centre. *Health Qual Life Outcomes* 11:207
8. Iacono Isidoro S, Salvaggio A, Lo Bue A, Romano S, Marrone O, Insalaco G (2015) Effect of obstructive sleep apnea diagnosis on health related quality of life. *Health Qual Life Outcomes* 13:68
9. Iacono Isidoro S, Salvaggio A, Lo Bue A, Romano S, Marrone O, Insalaco G (2016) Immediate effect of CPAP titration on perceived health related quality of life: a prospective observational study. *BMC Pulm Med* 16:172
10. Basoglu OK, Tasbakan MS (2017) Gender differences in clinical and polysomnographic features of obstructive sleep apnea: a clinical study of 2827 patients. *Sleep Breath* 20:1–9

11. Ye L, Pien GW, Weaver TE (2009) Gender differences in clinical manifestations of obstructive sleep apnea. *Sleep Med* 10:1075–1084
12. Young T, Peppard PE (2005) Clinical presentation of OSAS: gender does matter. *Sleep* 28:293–295
13. Gottlieb DJ, Whitney CW, Bonekat WH et al (1999) Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. *Am J Respir Crit Care Med* 159:502–507
14. Jacobsen JH, Shi L, Mokhlesi B (2013) Factors associated with excessive daytime sleepiness in patients with severe obstructive sleep apnea. *Sleep Breath* 17:629–635
15. Aurora RN, Collop NA, Jacobowitz O, Thomas SM, Quan SF, Aronson AJ (2015) Quality measures for the care of adult patients with obstructive sleep apnea. *J Clin Sleep Med* 11:357–383
16. Ye L, Pien G, Ratcliffe SJ, Weaver TE (2009) Gender differences in obstructive sleep apnea and treatment response to continuous positive airway pressure. *J Clin Sleep Med* 5:512–518
17. Eliasson AH, Kashani MD, Howard RS, Vernalis MN, Modlin RE (2015) Integrative cardiac health project registry. Fatigued on Venus, sleepy on Mars-gender and racial differences in symptoms of sleep apnea. *Sleep Breath* 19:99–107. <https://doi.org/10.1007/s11325-014-0968-y>
18. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, Davidson Ward SL, Tangredi MM, American Academy of Sleep Medicine (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 8:597–619
19. Grossi E, Mosconi P, Groth N, Niero M, Apolone G (2002) II Questionario psychological general well being, Questionario per la valutazione dello stato generale di benessere psicologico. Versione Italiana. Istituto di Ricerche Farmacologiche Mario Negri, Milan
20. Dupuy H (1984) The psychological general well-being (PGWB) index. In: Wenger NK, Mattson ME, Furburg CD, Elinson J (eds) Assessment of quality of life in clinical trials of cardiovascular therapies. Le Jacq Publishing, New York, pp 170–183
21. Apolone G, Mosconi P, Quattrociochi L, Gianicolo EA, Groth N, Ware JE (2005) Questionario sullo Stato di Salute SF-12. Versione italiana. Istituto di Ricerche Farmacologiche Mario Negri, Milan
22. Kodraliu G, Mosconi P, Groth N et al (2001) Subjective health status assessment: evaluation of the Italian version of the SF-12 short-form health survey. Results from the MiOS Project construction of scales and preliminary tests of reliability and validity. *J Epidemiol Biostat* 6:305–316
23. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 14:540–545
24. Vignatelli L, Plazzi G, Barbato A, Ferini-Strambi L, Manni R, Pompei F, D'Alessandro R, GINSEN (Gruppo Italiano Narcolessia Studio Epidemiologico Nazionale (2003) Italian version of the Epworth sleepiness scale: external validity. *Neurol Sci* 23:295–300
25. Kuna ST, Gurubhagavatula I, Maislin G, Hin S, Hartwig KC, McCloskey S, Hachadoorian R, Hurley S, Gupta R, Staley B, Atwood CW (2011) Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. *Am J Respir Crit Care Med* 183:1238–1244
26. Cohen J (1988) Statistical power analysis for the behavioral sciences, 2nd edn. Lawrence Erlbaum Associates, Mahwah
27. Cairns A, Poulos G, Bogan R (2016) Sex differences in sleep apnea predictors and outcomes from home sleep apnea testing. *Nat Sci Sleep* 8:197–205
28. Barsky AJ, Peekna HM, Borus JF (2001) Somatic symptom reporting in women and men. *J Gen Intern Med* 16:266–275
29. Sforza E, de Saint Hilaire Z, Pelissolo A, Rochat T, Ibanez V (2002) Personality, anxiety and mood traits in patients with sleep-related breathing disorders: effect of reduced daytime alertness. *Sleep Med* 3:139–145
30. Kang JM, Kang SG, Cho SJ, Lee YJ, Lee HJ, Kim JE, Shin SH, Park KH, Kim ST (2017) The quality of life of suspected obstructive sleep apnea patients is related to their subjective sleep quality rather than the apnea-hypopnea index. *Sleep Breath* 21:369–375
31. Billings ME, Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Zee PC, Redline S, Kapur VK (2014) Psychometric performance and responsiveness of the functional outcomes of sleep questionnaire and sleep apnea quality of life instrument in a randomized trial: the HomePAP study. *Sleep* 37:2017–2024
32. Zinchuk AV, Gentry MJ, Concato J, Yaggi HK (2016) Phenotypes in obstructive sleep apnea: a definition, examples, and evolution of approaches. *Sleep Med Rev*:1–11. <https://doi.org/10.1016/j.smrv.2016.10.002>
33. Baldwin CM, Kapur VK, Holberg CJ, Rosen C, Nieto FJ (2004) Associations between gender and measures of daytime somnolence in the sleep heart health study. *Sleep* 27:305–311
34. Silva GE, Goodwin JL, Vana KD, Quan SF (2016) Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest J Pulm Crit Care* 13:137–149
35. Weaver TE, Maislin G, Dinges DF, Bloxham T, George CFP, Greenberg H, Kader G, Mahowald M, Younger J, Pack AI (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30:711–719
36. Avlonitou E, Kapsimalis F, Varouchakis G, Vardavas CI, Behrakis P (2012) Adherence to CPAP therapy improves quality of life and reduces symptoms among sleep apnea syndrome patients. *Sleep Breath* 16:563–569
37. Olsen S, Smith S, Oei TP (2008) Adherence to continuous positive airway pressure therapy in obstructive sleep apnoea sufferers: a theoretical approach to treatment adherence and intervention. *Clin Psychol Rev* 28:1355–1371
38. Zhao YY, Wang R, Gleason KJ, BestAIR Investigators et al (2017) Effect of continuous positive airway pressure treatment on health-related quality of life and sleepiness in high cardiovascular risk individuals with sleep apnea: best apnea interventions for research (BestAIR) trial. *Sleep* 40:40. <https://doi.org/10.1093/sleep/zsx040>
39. Antic NA, Catcheside P, Buchan C, Hensley M, Naughton MT, Rowland S, Williamson B, Windler S, McEvoy RD (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34:111–119
40. Bjornsdottir E, Keenan BT, Eysteinsdottir B, Arnardottir ES, Janson C, Gislason T, Sigurdsson JF, Kuna ST, Pack AI, Benediktsson B (2015) Quality of life among untreated sleep apnea patients compared with the general population and changes after treatment with positive airway pressure. *J Sleep Res* 24:328–338
41. Gupta MA, Simpson FC, Lyons DC (2015) The effect of treating obstructive sleep apnea with positive airway pressure on depression and other subjective symptoms: a systematic review and meta-analysis. *Sleep Med Rev* 28:51–64

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