

# Continuous Positive Airway Pressure Improves Quality of Life in Women with Obstructive Sleep Apnea

## A Randomized Controlled Trial

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### Abstract

**Rationale:** Continuous positive airway pressure (CPAP) is the treatment of choice in patients with symptomatic obstructive sleep apnea (OSA). CPAP treatment improves quality of life (QoL) in men with OSA, but its role in women has not yet been assessed.

**Objectives:** To investigate the effect of CPAP on QoL in women with moderate to severe OSA.

**Methods:** We conducted a multicenter, open-label randomized controlled trial in 307 consecutive women diagnosed with moderate to severe OSA (apnea-hypopnea index,  $\geq 15$ ) in 19 Spanish sleep units. Women were randomized to receive effective CPAP therapy ( $n = 151$ ) or conservative treatment ( $n = 156$ ) for 3 months. The primary endpoint was the change in QoL based on the Quebec Sleep Questionnaire. Secondary endpoints included changes in daytime sleepiness, mood state, anxiety, and depression. Data were analyzed on an intention-to-treat basis with adjustment for baseline values and other relevant clinical variables.

**Measurements and Main Results:** The women in the study had a mean (SD) age of 57.1 (10.1) years and a mean (SD) Epworth Sleepiness Scale score of 9.8 (4.4), and 77.5% were postmenopausal. Compared with the control group, the CPAP group achieved a significantly greater improvement in all QoL domains of the Quebec Sleep Questionnaire (adjusted treatment effect between 0.53 and 1.33;  $P < 0.001$  for all domains), daytime sleepiness ( $-2.92$ ;  $P < 0.001$ ), mood state ( $-4.24$ ;  $P = 0.012$ ), anxiety ( $-0.89$ ;  $P = 0.014$ ), depression ( $-0.85$ ;  $P = 0.016$ ), and the physical component summary of the 12-item Short Form Health Survey ( $2.78$ ;  $P = 0.003$ ).

**Conclusions:** In women with moderate or severe OSA, 3 months of CPAP therapy improved QoL, mood state, anxiety and depressive symptoms, and daytime sleepiness compared with conservative treatment.

Clinical trial registered with [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02047071).

**Keywords:** obstructive sleep apnea; women; continuous positive airway pressure; quality of life; Quebec Sleep Questionnaire

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\*A complete list of members may be found before the beginning of the REFERENCES.

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## At a Glance Commentary

### Scientific Knowledge on the

**Subject:** Continuous positive airway pressure has been shown to improve quality of life, health status, and excessive daytime sleepiness in predominantly male cohorts, but its role in women has not yet been assessed. Given the different clinical manifestations of sleep apnea in both sexes, it remains unclear whether women's responses to sleep apnea symptoms are similar to those of men. Thus, women with sleep apnea are currently being treated in accordance with male criteria, which could be inappropriate.

### What This Study Adds to the

**Field:** To our knowledge, this is the first study of the role of continuous positive airway pressure therapy on the quality of life of women with sleep apnea. We have shown that 12 weeks of continuous positive airway pressure therapy improves quality of life, daytime sleepiness, mood state, and anxiety and depression symptoms compared with conservative treatment in middle-aged, nonsleepy women with moderate to severe sleep apnea.

Obstructive sleep apnea (OSA) is a common disorder in women, with a prevalence between 6 and 23% for moderate to severe OSA (1–3). Despite this high prevalence, research on female OSA is scant, and, so far, it has been taken for granted that there are no differences in the management of this sleep disorder between the two sexes. However, there are well-known sex differences in OSA, including a lower prevalence (4, 5) and different clinical manifestations in women, with more frequent “atypical” symptoms, such as depression, anxiety, insomnia, headache, and fatigue, and less

frequent complaints of excessive daytime sleepiness (EDS) (6–8). Sex differences have also been reported with regard to the role of sexual hormones, as well as to the severity of OSA, which is usually lower in women than in men (9–11), although women tend to present with greater impairment of both their quality of life (QoL) and their health status (12, 13). Differences regarding the pathophysiology of upper airway obstruction between men and women are controversial (14–16). Recent observational studies have also found a higher incidence of stroke and coronary heart disease and a greater risk of cardiovascular mortality in women with untreated OSA (17, 18).

Continuous positive airway pressure (CPAP) is the treatment of choice for patients with symptomatic OSA. Improvements in functional status and QoL with CPAP therapy have been well documented in clinical trials conducted in predominantly male samples (19–27). These studies, however, failed to examine sex differences, and consequently it remains unclear whether women's responses to the typical OSA symptoms, as well as to other, less specific complaints, such as depression, anxiety, mood disturbance, and excessive daytime sleepiness, are similar to those of men.

The lack of scientific evidence regarding the effects of CPAP in women with OSA precludes the development of specific protocols tailored to the characteristics of this population. Thus, women with OSA are currently being treated in accordance with criteria used for men, which could be inappropriate on account of the aforementioned sex differences. The objective of this study was to investigate whether CPAP treatment improves QoL and health status compared with conservative therapy in women with moderate to severe OSA. Some of the results of this study have been reported previously in the form of an abstract (28).

## Methods

### Design and Settings

A multicenter, open-label, randomized, and controlled trial of parallel groups with a final blind evaluation was conducted at 19 Spanish sleep units between February 2014 and February 2015. It was approved by the ethics committee of each participating center and registered with [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02047071). All the participants provided signed informed consent.

### Participants

Consecutive women between 18 and 75 years of age who were referred for suspicion of OSA were eligible if they were diagnosed with moderate to severe OSA (apnea–hypopnea index [AHI],  $\geq 15$ ). Exclusion criteria are detailed in the online supplement.

### Procedures

**Sleep study.** Every woman underwent home respiratory polygraphy with a device previously validated against polysomnography. Every sleep study was manually scored by skilled staff (*see online supplement*).

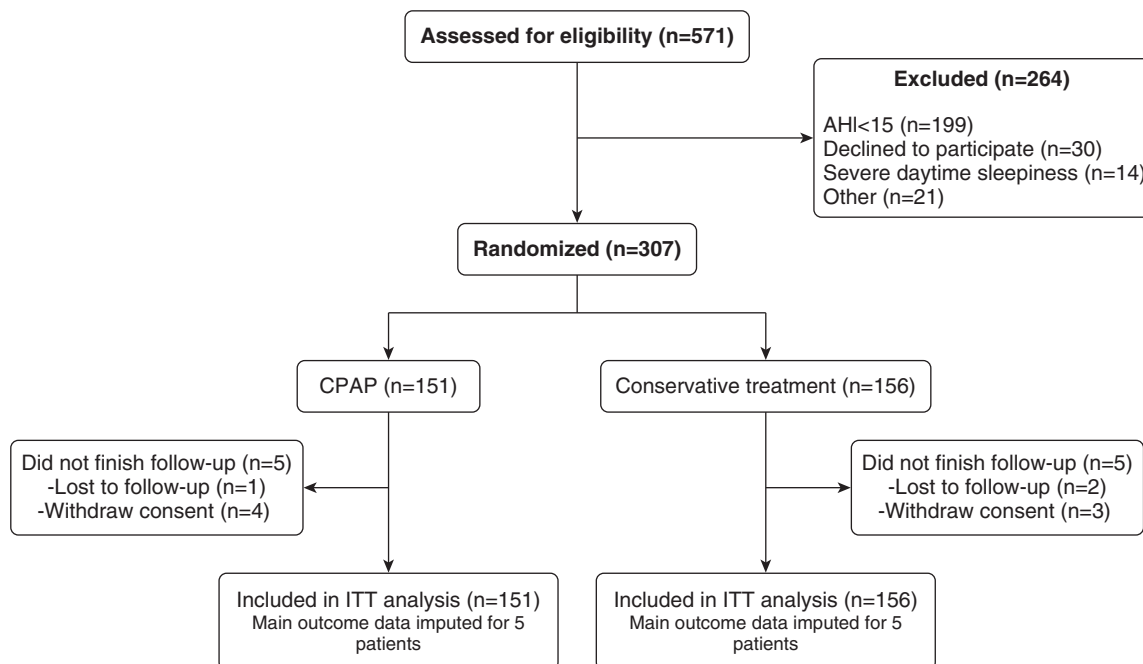
**Baseline visit.** After the diagnosis of OSA, all women completed the Quebec Sleep Questionnaire (QSQ), a specific sleep-related QoL questionnaire (29). We used the Epworth Sleepiness Scale (ESS) to quantify subjective daytime somnolence (30), the Abbreviated Profile of Mood States (POMS) to measure mood state (31), the Hospital Anxiety and Depression (HAD) questionnaire to assess anxiety and depression (32), and the brief version of the Short Form Health Survey (SF-12) to assess nonspecific health-related QoL (33). A validated Spanish-language version of each questionnaire was used in this study.

**Randomization.** Women with an AHI of 15 or higher were randomized to receive either CPAP or conservative treatment. All

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This article has an online supplement, which is accessible from this issue's table of contents at [www.atsjournals.org](http://www.atsjournals.org)



**Figure 1.** Flowchart of the study profile. AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; ITT = intention to treat.

the women received dietary and sleep hygiene counseling (*see* online supplement).

**CPAP titration.** Women randomized to the CPAP group were prescribed an

empiric CPAP level based on a validated predictive formula titration (34) for 2 weeks in an attempt to obtain a more accurate, and possibly lower, long-term pressure

setting, and also to assist with CPAP acclimatization, before they underwent a titration night with use of an automatic CPAP device to determine the final

**Table 1.** Baseline Characteristics of the Women Included in the Study

Variables	Whole Group (n = 307)	Control Group (n = 156)	CPAP Group (n = 151)	P Value
Age, yr	57.1 (10.1)	55.5 (10.3)	58.8 (9.6)	0.005
BMI, kg/m <sup>2</sup>	33.7 (29.0–38.5)	33.8 (29.6–39.1)	33.5 (28.9–37.6)	0.033
Neck circumference, cm	37.5 (35.0–40.0)	38.0 (36.0–40.4)	37.0 (35.0–40.0)	0.109
Waist-to-hip ratio	0.90 (0.86–0.94)	0.90 (0.86–0.95)	0.90 (0.85–0.94)	0.209
Menopause	238 (77.5)	117 (75.0)	121 (80.1)	0.339
Physical activity <30 min/d	160 (52.1)	83 (53.2)	77 (51.0)	0.732
Sleep duration, h/d	7.0 (6.0–8.0)	7.5 (6.0–8.0)	7.0 (6.0–8.0)	0.363
Smoker, current or former	129 (42.0)	74 (47.4)	55 (36.4)	0.064
Depression	106 (34.5)	58 (37.2)	48 (31.8)	0.339
Anxiety	86 (28.0)	44 (28.2)	42 (27.8)	1.000
Use of sedative drugs	78 (25.4)	36 (23.1)	42 (27.8)	0.361
Antidepressant therapy	87 (28.3)	45 (28.8)	42 (27.8)	0.899
Apnea-hypopnea index	32.0 (22.6–48.5)	31.0 (20.3–46.8)	35.1 (24.3–50.0)	0.431
Oxygen desaturation index	32.9 (22.1–49.5)	30.2 (21.0–49.0)	34.5 (23.3–49.7)	0.662
Epworth Sleepiness Scale score	9.8 (4.4)	9.4 (4.6)	10.2 (4.2)	0.142
QSQ hypersomnolence	5.0 (1.3)	5.0 (1.4)	5.0 (1.3)	0.831
QSQ diurnal symptoms	4.1 (1.5)	4.1 (1.5)	4.2 (1.5)	0.756
QSQ nocturnal symptoms	4.1 (1.3)	4.1 (1.3)	4.1 (1.3)	0.935
QSQ emotions	4.7 (1.3)	4.7 (1.3)	4.7 (1.3)	0.905
QSQ social interaction	4.8 (1.4)	4.8 (1.5)	4.7 (1.4)	0.589
HAD depression	6.3 (4.4)	6.6 (4.3)	5.9 (4.4)	0.198
HAD anxiety	8.9 (4.2)	8.7 (4.2)	9.0 (4.2)	0.531
POMS	28.0 (12.0–43.0)	29.5 (13.0–45.8)	26.0 (12.0–41.0)	0.366
SF-12 Physical summary	39.1 (11.0)	39.3 (10.9)	38.9 (11.1)	0.756
SF-12 Mental summary	44.6 (11.5)	44.1 (12.2)	45.1 (10.7)	0.425

*Definition of abbreviations:* BMI = body mass index; CPAP = continuous positive airway pressure; HAD = Hospital Anxiety and Depression questionnaire; POMS = Profile of Mood States; QSQ = Quebec Sleep Questionnaire; SF-12 = 12-item Short Form Health Survey. Data are expressed as mean (SD), median (interquartile range), or number of patients (percent).

treatment pressure (see online supplement).

**Follow-up.** Follow-up evaluations were done at 4 and 12 weeks (see online supplement). Every woman completed the QSQ, POMS, ESS, HAD, and SF-12 questionnaires at her last medical appointment.

**Statistical analysis.** The results are expressed as mean (SD) or median (interquartile range [IQR]) for continuous variables and number of patients (percent) for categorical variables. The primary endpoint was the change in the QSQ domains at 12 weeks compared with baseline in the CPAP group versus the control group. Secondary endpoints included changes in the scores of the ESS, POMS, HAD, and SF-12 questionnaires. The sample size was calculated on the basis of a clinically significant improvement in all the domains of the QSQ, using the domain that needed the largest sample size (emotions). To obtain at least a 1.1-unit change in the emotions domain between groups at the end of the follow-up, considering an SD of 2.6, an  $\alpha$  error rate of 5%, and a statistical power of 90%, and assuming a dropout rate of 15%, 149 patients would be necessary in each arm.

The intergroup comparison of the changes in QSQ and other QoL questionnaire scores were assessed by analysis of covariance with adjustments for baseline values, age, body mass index (BMI), anxiety, depression, and intake of sedative drugs. The analyses were performed on an intention-to-treat basis.

Pearson's correlations and scatterplots were used to investigate whether there were any relationships between hours of CPAP use and changes in the QSQ domains. We conducted a sensitivity analysis to separately investigate the effect of CPAP therapy in the QSQ domains in the group of women with severe OSA (AHI,  $\geq 30$ ) and in the group of women with moderate OSA (AHI, 15–29.9).

Two-tailed *P* values less than 0.05 were considered significant. The IBM SPSS 19.0 statistical software package (IBM, Armonk, NY) was used for data processing and analysis. The statistical analyses were performed using a blind evaluation of the study groups. Additional information on the statistical analyses is provided in the online supplement.

## Results

Two hundred sixty-four of the 571 consecutive women assessed for eligibility had exclusion criteria or declined participation, and 307 were randomized, 151 to CPAP and 156 to conservative treatment (Figure 1). Only 10 women (5 in each group) did not complete the follow-up, mainly because they withdrew consent.

The women had a mean age of 57.1 (SD, 10.1) years (77.5% were postmenopausal), a mean ESS score of 9.8 (SD, 4.4), a median BMI of 33.7 (IQR, 29.0–38.5) kg/m<sup>2</sup>, and a median AHI of 32.0 (IQR, 22.6–48.5). The average effective CPAP was 10.3 (2.3) cm H<sub>2</sub>O, and the average residual AHI was 2.0 (IQR, 0.8–4.2). Twelve women (7.9%) needed titration by attended polysomnography because the auto-CPAP titration was not adequate.

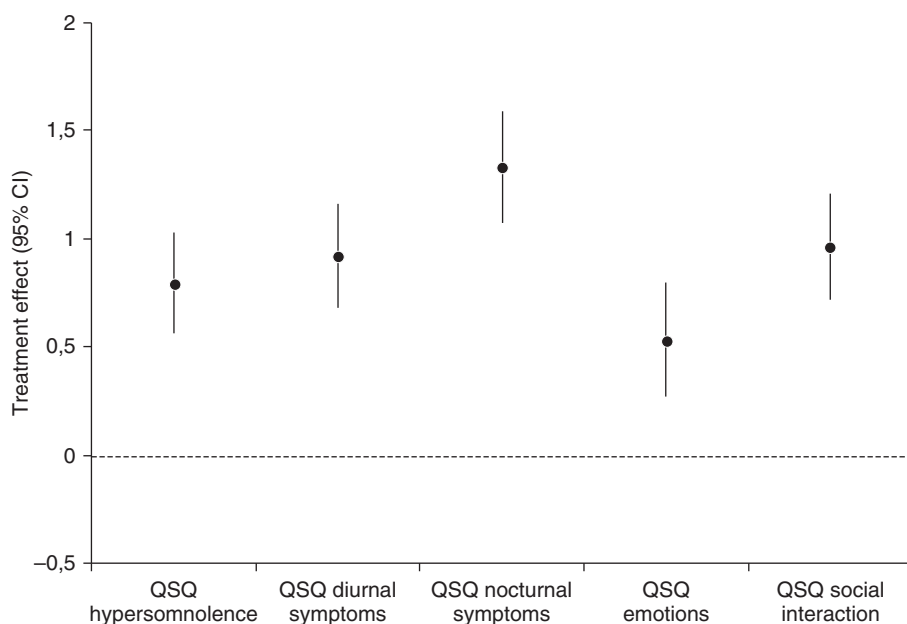
The baseline characteristics, QoL scores, and OSA severity did not differ between groups, except for age and BMI (Table 1). Women in the CPAP group were older and less obese than those in the

control group. No significant change in weight was observed in the CPAP and control groups over the course of the study.

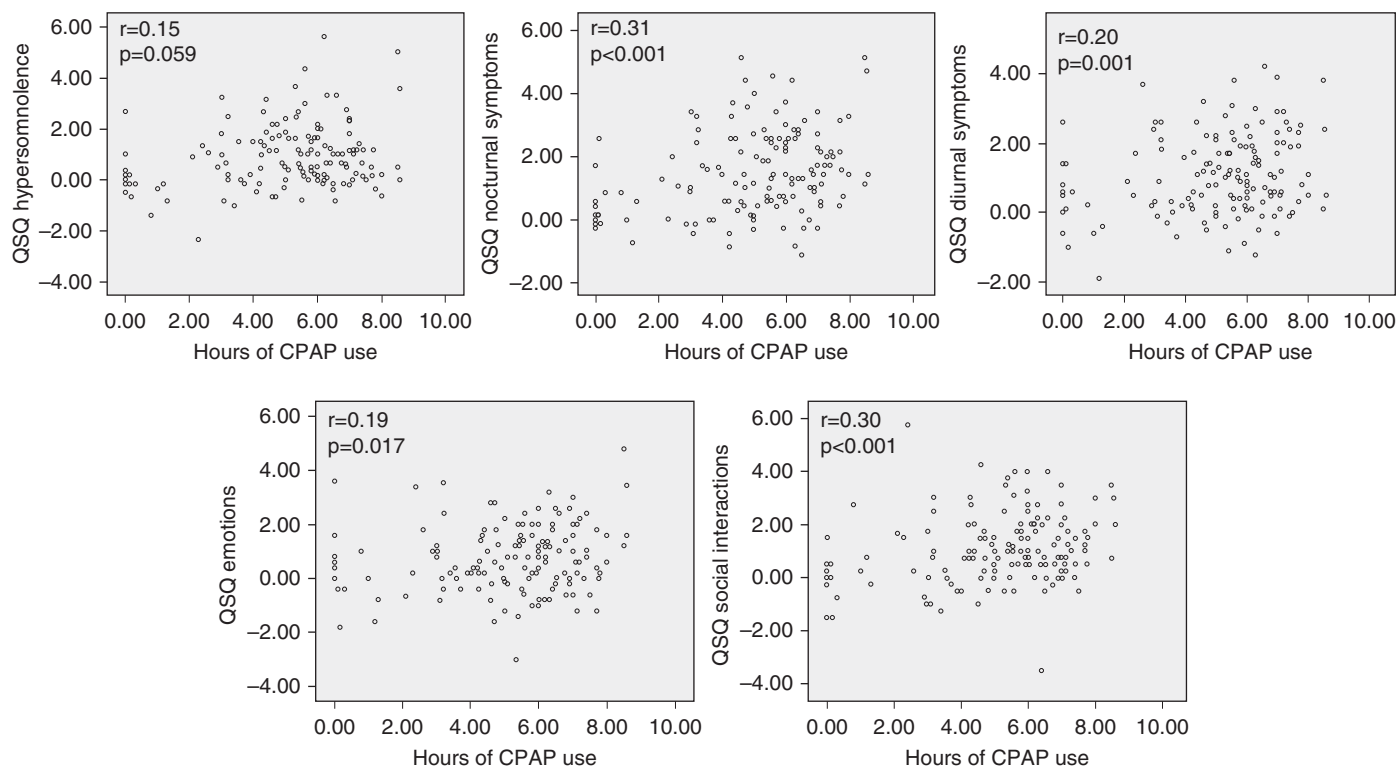
In the CPAP group, the mean nightly use of the device was 4.8 (2.5) h/d. Among the 151 women randomized to the CPAP group, 8 did not tolerate the device and did not even begin CPAP therapy, 2 additional women dropped out, and 141 women wore the device until the end of the follow-up. None of the patients in the control arm began CPAP therapy during the 12 weeks of the study.

### Primary Endpoint

After 12 weeks of follow-up, the CPAP group achieved a significantly greater improvement than the control group in all QoL domains of the QSQ ( $P < 0.001$  for all domains) (Figure 2; Table E1 in the online supplement). There was a moderate but significant correlation between CPAP treatment adherence and improvement in the diurnal symptom, nocturnal symptom, emotion, and social interaction domains of the QSQ (Figure 3). The correlation with the hypersomnolence domain was nearly significant. For every 1-hour increase in CPAP treatment adherence, the



**Figure 2.** Effect of continuous positive airway pressure therapy on the Quebec Sleep Questionnaire (QSQ) domains. Adjusted treatment effects and 95% confidence intervals (CIs) (adjusted by baseline values, age, body mass index, anxiety, depression, and intake of sedative drugs) of continuous positive airway pressure versus conservative treatment at the end of follow-up compared with baseline: hypersomnolence, 0.79 (95% CI, 0.56–1.03;  $P < 0.001$ ); diurnal symptoms, 0.92 (95% CI, 0.68–1.16;  $P < 0.001$ ); nocturnal symptoms, 1.33 (95% CI, 1.07–1.59;  $P < 0.001$ ); emotions, 0.53 (95% CI, 0.27–0.8;  $P < 0.001$ ); social interaction, 0.96 (95% CI, 0.72–1.21;  $P < 0.001$ ).



**Figure 3.** Pearson correlation between hours of continuous positive airway pressure (CPAP) use and changes in the Quebec Sleep Questionnaire (QSQ) domains.

improvement in the domains of the QSQ were 0.12 for hypersomnolence, 0.12 for diurnal symptoms, 0.20 for nocturnal symptoms, 0.10 for emotions, and 0.16 for social interactions.

### Secondary Endpoints

After 12 weeks of follow-up, and compared with the control group, the CPAP group achieved a significantly greater improvement in daytime sleepiness, mood state, anxiety, and depression symptoms, as well as in the physical component summary of the SF-12 (Figure 4). No differences between groups were found in the mental component summary of the SF-12.

### Effect of CPAP Therapy on QSQ Scores of Women with Moderate to Severe OSA

CPAP therapy significantly improved all the domains of the QSQ ( $P < 0.05$  for all domains) compared with the control group in women with severe OSA and those with moderate OSA (AHI  $\geq 30$  and AHI 15–29.9, respectively). This benefit was greater for women with severe OSA than for those with moderate OSA for the nocturnal symptom, social interaction, and

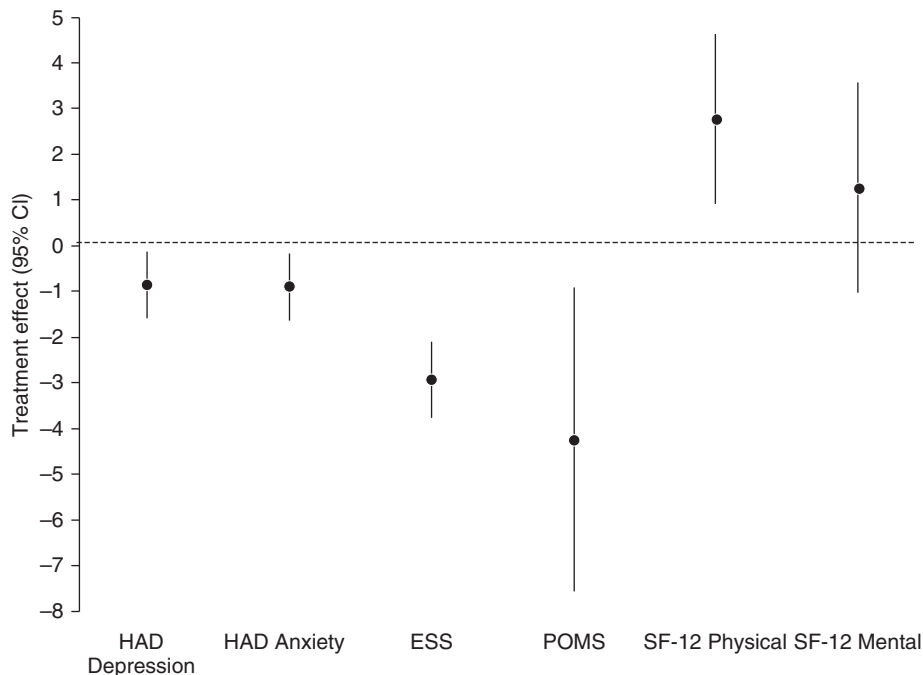
hypersomnolence domains, but it was similar for the diurnal symptom and emotion domains (Figure 5).

## Discussion

To our knowledge, this is the first randomized controlled trial with an assessment of the effect of CPAP treatment on different aspects of QoL in women with moderate to severe OSA. Our findings show that 12 weeks of CPAP therapy improved different QoL domains (mood state, daytime sleepiness, and anxiety and depressive symptoms) compared with conservative treatment. This improvement was achieved not only in women with severe OSA but also in those with moderate OSA. These beneficial effects increased with greater CPAP treatment adherence.

It is well known that OSA differs between the sexes in terms of prevalence, severity, and clinical presentation (1, 3, 4, 6–10, 12–14). However, little attention has been paid to the role of CPAP therapy on health status in women with OSA, as it has been taken for granted that the effects of this therapy would be similar to those

found in men. Randomized controlled trials in which researchers have investigated the effect of CPAP treatment on sleepiness and QoL have been conducted predominantly or exclusively in men (19–21, 23–27), and investigators in the few studies involving mixed samples did not stratify their results by sex (22, 35). The only study in which researchers have specifically investigated the effect of CPAP therapy on women's health status was an observational study conducted in 152 men and 24 women with OSA (36). After 3 months of CPAP treatment, QoL, functional status, daytime sleepiness, mood disturbance, and neurobehavioral performance significantly improved in both men and women. Observational studies also suggest that CPAP therapy may reduce depressive symptoms in women with OSA (37). In a recent economic analysis of the cost-effectiveness and cost per quality-adjusted life-year associated with CPAP treatment on the basis of generic health-related QoL instruments and cardiovascular risks, researchers demonstrated that CPAP therapy is cost-effective compared with conservative care and dental devices in men with OSA (38). Although similar results



**Figure 4.** Effect of continuous positive airway pressure therapy on depression, anxiety, nonspecific health-related quality of life, daytime sleepiness, and mood state. Adjusted treatment effects and 95% confidence intervals (CIs) (adjusted by baseline values, age, body mass index, anxiety, depression, and intake of sedative drugs) of continuous positive airway pressure versus conservative treatment at the end of follow-up compared with baseline: HAD Depression,  $-0.85$  (95% CI,  $-1.55$  to  $-0.15$ ;  $P=0.016$ ); HAD Anxiety,  $-0.89$  (95% CI,  $-1.61$  to  $-0.18$ ;  $P=0.014$ ); ESS,  $-2.92$  (95% CI,  $-3.73$  to  $-2.11$ ;  $P<0.001$ ); POMS,  $-4.24$  (95% CI,  $-7.54$  to  $-0.94$ ;  $P=0.012$ ); SF-12 Physical,  $2.78$  (95% CI,  $0.96$ – $4.61$ ;  $P=0.003$ ); SF-12 Mental,  $1.27$  (95% CI,  $-1.01$  to  $3.56$ ;  $P=0.27$ ). HAD = Hospital Anxiety and Depression questionnaire; ESS = Epworth Sleepiness Scale; POMS = Abbreviated Profile of Mood States; SF-12 = 12-item Short Form Health Survey.

were obtained for a hypothetical cohort of women, the different characteristics of OSA between the sexes suggest that the economic value of this treatment in women is also likely to be different.

In our study, we used the QSQ, a health-related QoL questionnaire validated for patients with OSA and sensitive to treatment-induced changes (29). We have shown that 3 months of CPAP therapy achieved a statistically significant greater improvement than conservative OSA therapy in the five domains that compose this questionnaire (hypersomnolence, diurnal symptoms, nocturnal symptoms, emotions, and social interactions), demonstrating that CPAP treatment improves different aspects of QoL related to OSA. We also observed a dose–response relationship between QoL scores and increasing CPAP treatment adherence, suggesting that this benefit increases with better adherence, as previously reported in predominantly male cohorts (39).

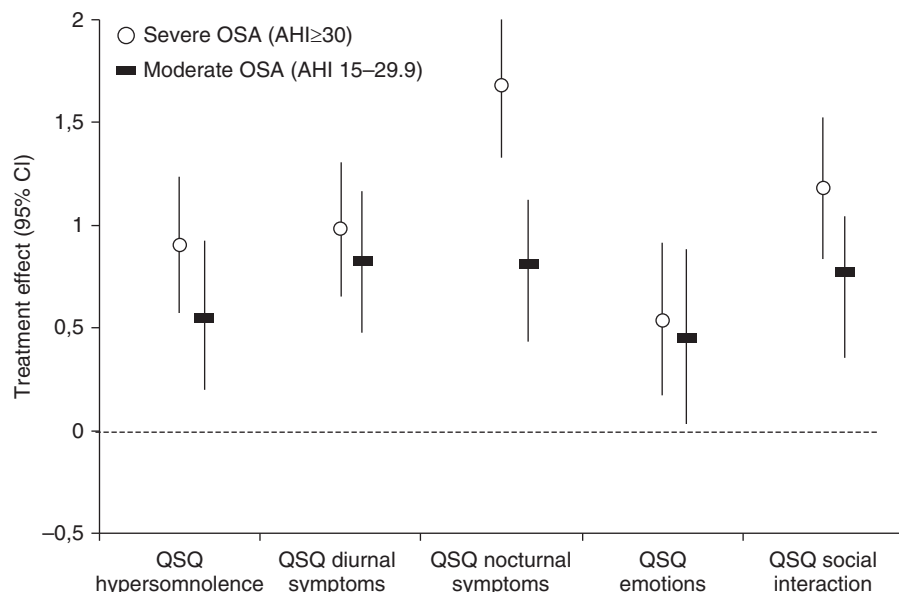
Remarkably, this improvement was not restricted to women with severe OSA but also applied to those with moderate OSA, although the improvement achieved was usually smaller in the latter group.

Despite the statistically significant improvement obtained, these differences did not, however, reach the clinical significance level published by the authors of the QSQ, except for the domain of nocturnal symptoms (29). There are two reasons for this. First, the validation of the clinically significant differences was originally undertaken in a population in which women were underrepresented, with 19 treated and 9 untreated men and only 8 treated women, so it is uncertain whether these minimum differences can be applied to women. Second, unlike most studies addressing the role of CPAP therapy in QoL and health status, in which investigators usually select patients with symptomatic OSA (19, 20, 24, 26, 27), the only enrollment criterion in our study was

an AHI of 15 or higher, regardless of symptoms. The reason is that no cornerstone symptom of OSA has been identified for women, with most complaints being quite unspecific. In fact, OSA may provoke a wide range of health status consequences in women, including depression, anxiety, mood disturbance, fatigue, and many more. For this reason, to address the effect of treatment on a wide range of health status aspects, we chose not to restrict enrollment to women with one or more specific complaints. Consequently, it is probable that some asymptomatic women with nonimpaired QoL were enrolled, reducing the effect of CPAP treatment on the whole sample. This characteristic is also a strength of our study because our results are highly generalizable to women diagnosed with moderate to severe OSA in sleep laboratories, regardless of the referred complaints.

Remarkably, in our sample, CPAP treatment led to a statistically and clinically significant decrease in ESS scores compared with conservative treatment. The adjusted mean difference in the ESS scores between both groups was nearly 3 points, a figure similar to or even greater than those reported in some studies of sleepy patients (20, 22, 26). This reduction was obtained even though the women in our study were basically nonsleepy (average ESS of 9.8 for the whole group). The ESS has been reported to be a less sensitive measure of subjective sleepiness in females than in males (40). Although researchers in another population-based study did not find any association between OSA and increased subjective sleepiness measured with the ESS in females of any age (41), our results suggest that CPAP treatment substantially improves daytime sleepiness in women, even if they do not present with high ESS scores.

Among patients with a similar OSA severity, women usually have poorer perceived health status than men (13), with a more disturbed mood state and a higher prevalence of both depression and anxiety (6, 8, 36). Researchers in several studies have reported a beneficial effect of CPAP therapy on these outcomes (36, 42–44), but they enrolled predominantly male cohorts or did not use a randomized controlled design. In our study, we have shown that CPAP therapy also improved mood state as well as symptoms of depression and anxiety compared with conservative treatment, suggesting that OSA broadly impairs health



**Figure 5.** Effect of continuous positive airway pressure therapy on the Quebec Sleep Questionnaire (QSQ) domains, according to obstructive sleep apnea (OSA) severity. Adjusted treatment effects and 95% confidence interval (CIs) (adjusted by baseline values, age, body mass index, anxiety, depression, and intake of sedative drugs) of continuous positive airway pressure versus conservative treatment, at the end of the follow-up compared with baseline, in the groups of women with moderate and severe OSA. Data were analyzed on an intention-to-treat basis. For the group with moderate OSA (apnea–hypopnea index [AHI], 15–29.9): hypersomnolence, 0.56 (95% CI, 0.20–0.92;  $P=0.002$ ); diurnal symptoms, 0.85 (95% CI, 0.45–1.24;  $P<0.001$ ); nocturnal symptoms, 0.85 (95% CI, 0.46–1.24;  $P<0.001$ ); emotions, 0.47 (95% CI, 0.07–0.88;  $P=0.022$ ); social interaction, 0.74 (95% CI, 0.36–1.11;  $P<0.001$ ). For the group with severe OSA (AHI,  $\geq 30$ ): hypersomnolence, 0.90 (95% CI, 0.58–1.23;  $P<0.001$ ); diurnal symptoms, 0.98 (95% CI, 0.66–1.30;  $P<0.001$ ); nocturnal symptoms, 1.68 (95% CI, 1.33–2.03;  $P<0.001$ ); emotions, 0.54 (95% CI, 0.18–0.91;  $P=0.003$ ); social interaction, 1.18 (95% CI, 0.84–1.52;  $P<0.001$ ).

status in women and that these complaints may be reversed by CPAP therapy.

Our study has several limitations. First, the control group was not blinded because no placebo was used. This design has previously been used by other authors (19, 21, 35, 45). We did not use a sham CPAP because we do not believe it is a true placebo. Excessive air leaking, low air pressure, and persistence of symptoms such as snoring would make patients realize that they were not receiving an effective treatment, especially in a study with several months of follow-up. In fact, in many of the trials in which investigators have employed a sham CPAP, adherence was significantly lower than with true CPAP, suggesting that patients were somehow aware of these pitfalls (22, 25, 46, 47). Second, women were diagnosed by means of respiratory polygraphy instead of conventional polysomnography, and CPAP was titrated with an automated device. The authors of the original description of the QSQ,

however, found no differences in the impact scores obtained from patients diagnosed using home oximetry (a much less accurate tool than respiratory polygraphy) and from those in whom the diagnosis was made with polysomnography (48). Third, the test used for the primary endpoint, the QSQ, has not been validated in women. Unfortunately, none of the other QoL questionnaires, such as the Functional Outcomes of Sleep Questionnaire and the Sleep Apnea Quality of Life Index, have been validated for women either. Fourth, our cohort was composed predominantly of middle-aged postmenopausal women. Because the number of young premenopausal women was small and this group may have a different clinical profile, we cannot rule out that the effect of CPAP treatment on some of the outcomes measured may vary in this particular group of women. Fifth, despite blinded randomization, women in the CPAP group were older and less obese than those in the

control group. We believe that these differences were due to chance because the rest of the variables, including other anthropometric measures such as neck circumference and waist-to-hip ratio as well as the QoL test scores, were comparable in both groups. To control for this limitation, all the analyses were adjusted for age and BMI. Finally, we did not analyze any objective variables in this study, but QoL is usually assessed in daily clinical practice by means of subjective tests, and most of these were used in this study. We did not perform a cost-effectiveness analysis of CPAP treatment that may have reinforced the benefits of this therapy.

In summary, our study provides, for the first time, high-quality evidence demonstrating that CPAP treatment is effective in improving a wide range of health status outcomes in a group of middle-aged, postmenopausal, nonsleepy women with moderate to severe OSA. CPAP treatment improved different QoL domains associated with sleep-disordered breathing, as well as other subjective health-related outcomes such as daytime sleepiness, mood state, and depression and anxiety complaints. These improvements were obtained not only in women with severe OSA but also in those with moderate OSA severity. Because in our study women were included regardless of clinical complaints or previous QoL selection criteria, we believe that these results may be generalized to women diagnosed with moderate to severe OSA in sleep laboratories. ■

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