Gender Differences in Obstructive Sleep Apnea and Treatment Response to Continuous Positive Airway Pressure

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Objectives: Whether gender differences exist in clinical manifestations of obstructive sleep apnea (OSA) and whether women’s responses to continuous positive airway pressure (CPAP) are similar to those of men are critical areas of exploration in sleep disordered breathing. This exploratory analysis addressed these questions by examining gender differences over a wide range of clinical outcomes at baseline and in response to CPAP in participants with severe OSA.

Methods: Data from 152 men and 24 women who participated in a multicenter CPAP effectiveness study were analyzed. Gender differences in functional status (functional outcomes of sleep questionnaire, sickness impact profile), daytime sleepiness (epworth sleepiness scale, multiple sleep latency test), mood disturbance (profile of mood states), apnea symptoms (multivariable apnea prediction index), and neurobehavioral performance (psychomotor vigilance task) were examined. Treatment response was examined by the change in each outcome from baseline to 3 months after treatment.

Results: Despite similar age, body mass index, and apnea-hypopnea index, women reported significantly lower functional status, more subjective daytime sleepiness, higher frequency of apnea symptoms, more mood disturbance, and poorer neurobehavioral performance compared to men at baseline. CPAP treatment significantly improved functional status and relieved symptoms for both genders. The magnitude of improvement in each clinical outcome did not vary by gender.

Conclusions: Women with OSA showed greater impairment in daytime functioning and symptoms than men. Both genders benefit from CPAP treatment. Adequately powered studies considering possible referral and response bias are necessary to examine gender differences in OSA clinical manifestations and response to CPAP treatment.

Keywords: Obstructive sleep apnea, CPAP, gender differences, functional status, daytime sleepiness, treatment response

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Obstructive sleep apnea (OSA) is a common sleep related breathing disorder characterized by episodic nocturnal collapse of the upper airway resulting in excessive daytime sleepiness,1 mood disturbances,2 deficits in neurobehavioral performance,3 and deterioration in functional status and quality of life.4 Until fairly recently, OSA was viewed as a “male” disease, but recent studies in the general population demonstrate that this condition is not rare in women, with at least 2% of middle-aged women having OSA.5,6 However, OSA is undiagnosed in more than 90% of women.7 The paucity of data regarding OSA in women and the limited understanding of gender differences in OSA may be the root of the gender bias observed in this syndrome.8

Understanding gender differences in OSA is a critical area of exploration. Recent studies examining gender differences in upper airway anatomy and function,9 polysomnographic features,10 symptom presentation,11-13 and morbidity and health care utilization14 have added to the growing body of knowledge in this area. However, gender differences in functional status, a component of quality of life used to describe the effect of an illness on the patient’s ability to conduct everyday tasks, has not been well investigated. Whether gender differences exist in neurobehavioral performance and important symptoms of OSA, such as excessive daytime sleepiness, still remains inconclusive. Moreover, less effort has been dedicated to identifying how gender affects the response to treatment for OSA, especially the primary treatment option, continuous positive airway pressure (CPAP), posing a critical challenge to appropriate management. Improvements in daytime sleepiness, mood disturbance, functional status, and neuropsychological performance following CPAP treatment have been documented in clinical trials.15 However, no gender-specific results have been reported, and it remains unclear whether women’s responses to CPAP are similar to those of men.

To address these questions, we conducted an exploratory analysis using data from a multisite effectiveness study of CPAP therapy for patients with OSA.16 Gender differences were examined in a wide range of clinical outcomes, including functional status, daytime sleepiness, mood state, apnea symptoms, and neurobehavioral performance. As these outcomes included...
both physical health and social functioning, gender differences, which refers to patients’ experiences and societal influences, rather than sex differences, which primarily refers to biological differences, was the preferred term used in this study. This preliminary investigation sought to contribute to our understanding of gender differences in OSA, and to explore whether gender differences exist in response to CPAP treatment.

METHODS

This report is a secondary analysis of data from a multisite study. Participants were patients who had been referred to one of 7 sleep centers in the United States and Canada for evaluation of a sleep problem during a 50-month period from 1996 to 2001, inclusively. The study was approved by the institutional review board at each institution, and written informed consent was provided by each subject.

Procedure

Methodology of this study has been reported previously. Briefly, sleep apnea patients who met inclusion criteria (age 21 to 60 years; apnea hypopnea index [AHI] ≥ 15, and a candidate for CPAP treatment) were recruited at 7 clinical sites. Participants were excluded if they had any coexisting sleep disorder, used sedative or hypnotic medication, had a history of coexisting pulmonary disease, cognitive heart failure, cerebrovascular accident, psychiatric illness, or were older than 60 years (because common age-related changes such as central apneas can affect response to treatment). Prior to in-laboratory, overnight, diagnostic polysomnogram (PSG), after providing informed written consent, participants completed a scheduled test battery. This report is limited to data from the tests of functional status (functional outcomes of sleep questionnaire [FOSQ]); sickness impact profile scale [SIP]); daytime sleepiness (Epworth Sleepiness Scale [ESS]; multiple sleep latency test [MSLT]); mood (profile of mood states [POMS]); apnea symptoms (multivariable apnea prediction [MAP] index), and neurobehavioral performance (psychomotor vigilance task [PVT]). After the day of testing, participants were instructed in the use of CPAP and provided devices with a monitor that contained a microprocessor recording daily (24 hours) mask-on use. Adherence was assessed as the mean hours of daily use over the entire follow-up period. No data on a functioning monitor indicated no use. Following 3 months of treatment, participants returned to the sleep center where they underwent the same testing as they did prior to treatment. Data from 176 patients (152 men and 24 women) who participated in the multicenter study were analyzed.

Measurements

Functional Status

Functional status was measured by the FOSQ. The FOSQ is a 30-item self-report, disease-specific measure designed to assess the effect of excessive sleepiness on daily functional ability. It has established content validity, test-retest reliability (r = 0.90), and internal consistency (α = 0.96). There are 5 subscales: activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcomes. The FOSQ total score is the computed mean of the subscale scores. The potential range for each subscale score is 1–4, with a total score of 5–20. Lower scores on the FOSQ indicate greater functional disability.

The SIP was administered as a generic measure of daily function and quality of life. It consists of 12 physical and psychosocial subscales, and is a valid and reliable, frequently used questionnaire. An overall SIP score of 0 is perfect health or functioning, and a higher score denotes poorer function.

Daytime Sleepiness

Subjective sleepiness was assessed using the ESS. The ESS is a commonly used, reliable self-administered questionnaire with items about the likelihood of dozing or falling asleep in 8 potentially soporific situations. A 4-point Likert scale ranges from never dozing (score 0) to a high chance of dozing (score 3). Scores > 10 on this 0–24 scale have often been used to define abnormal subjective sleepiness. At this cut point, the ESS has a sensitivity of 93.5% and a specificity of 100% for distinguishing pathological from normal sleepiness.

Objective sleepiness was measured using the MSLT. The MSLT polysomnographically measures the time required for the participant to fall asleep in a 20-min period when attempting to do so. Nap opportunities were administered at 2-h intervals during the test day for a total of 4 test bouts. The average latency time to sleep stage 1 was calculated across the test bouts. Sleep onset latency ≥ 10 min is considered normal or non-sleepy.

Mood State

Mood was measured by the POMS questionnaire. The POMS consists of 65 adjectives; subjects rate themselves on each by how they feel “today” using a 5-point scale (“not at all” to “extremely”). There are 6 subscales: tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment. The total mood disturbance (TMD) score was used to represent the global mood state.

Apnea Symptoms

The apnea symptom score, a subscale of the MAP Index, was used to evaluate classic apnea symptoms such as loud snoring, snorting, or gasping and apneas during sleep in the last month. Scores representing the frequency of symptoms range from 0 (never) to 4 (always) and are computed by averaging non-missing responses.

Neurobehavioral Performance

Neurobehavioral performance was measured by the PVT. The PVT is a task designed to evaluate the ability to sustain attention and respond in a timely manner to salient signals presented at random intervals over a 10-min test. For this report, 2 PVT metrics were evaluated: the mean reaction time in milliseconds and the number of lapses (i.e., reaction time ≥ 500 milliseconds), which are the 2 commonly used variables derived from the PVT to represent neurobehavioral performance.
Statistical Analyses

The sample characteristics were evaluated using summary statistics with values given as means and standard deviations, medians and interquartile ranges, or proportions as appropriate. To ensure normality, natural logarithm transformations were applied for PVT number of lapses, and reciprocal transformations were applied for PVT reaction time. Baseline impairment between genders was compared by independent-sample t tests, Mann-Whitney U, χ² tests or Fisher exact tests, as appropriate. Paired t-tests or nonparametric Wilcoxon matched-pairs tests were used to assess changes in scores from baseline to post-treatment within each gender group. T tests or Mann-Whitney U tests were used to compare change scores between genders.

SPSS Version 15.0 (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. Two-sided p-values of 0.05 were considered statistically significant.

RESULTS

Participant Characteristics

One hundred and seventy-six patients (152 men and 24 women) met the study inclusion criteria and participated in the multicenter study. Following 3 months of CPAP treatment, 10 participants (all men) did not return for follow-up testing; and CPAP adherence data for 17 participants (12 men and 5 women) were lost due to technical reasons (monitor transformer breakage, monitor battery failure, or corruption of electronic data during data transfer). The demographic characteristics for these participants and their degree of OSA are summarized in Table 1. In general, the sample was predominantly Caucasian (85.8%), male (86.4%), middle-aged (46.7 ± 8.8 years), and quite obese (BMI 38.0 ± 8.2 kg/m²). The average AHI for the entire sample was 63.9 events per hour of sleep. One hundred forty-four (81.8%) participants had an AHI > 30, indicating severe OSA.

Gender Differences at Baseline

Baseline scores in functional status, daytime sleepiness, mood, apnea symptoms, and neurobehavioral performance are shown and compared between genders in Table 2. The age, BMI, and AHI were not statistically different between men and women. The FOSQ total score was significantly lower in women (12.8 vs. 15.0, p = 0.002, effect size = 0.72), indicating poorer overall functional status. When individual subscales of the FOSQ were examined, women showed lower activity level (2.4 vs. 2.8, p = 0.004, effect size = 0.65) and less general productivity (3.0 vs. 3.3, p = 0.050, effect size = 0.44). Similarly, higher SIP global scores were observed in women (11.9 vs. 8.4, p = 0.040, effect size = 0.46), representing greater overall disability.

Women reported an average ESS score 2.3 points higher than men (16.8 vs. 14.5, p = 0.032, effect size = 0.49). However, the sleep latency time measured by the MSLT was not statistically different between men and women (5.8 vs. 7.0 minutes, p = 0.322). Defined by ESS scores > 10 and sleep latency time < 10 minutes, respectively, 79.3% of all participants had subjective excessive daytime sleepiness, and 73.8% had objective sleepiness. Significantly higher proportions of women had subjective daytime sleepiness compared to men at baseline (95.5% vs 76.9%, Fisher exact p = 0.049), but proportions of objective sleepiness were not significantly different between genders (85.7% vs. 72.2%, χ² = 1.75, p = 0.186).

Women also reported higher TMD scores (21.0 vs. 11.9, z = −2.68, p = 0.007) indicating greater overall mood disturbances and higher apnea symptom scores (3.4 vs. 3.0, p = 0.042, effect size = 0.36). In addition, women had longer reaction times (379.9 vs. 311.1 milliseconds, p = 0.001, effect size = 0.69) and more total lapses (9.0 vs. 4.6, p = 0.008, effect size = 0.65) derived from the PVT, indicating a poorer neurobehavioral performance. One female subject had a mean PVT reaction time at 1828.6 milliseconds, which was exceptional high compared to other subjects. Analyses were conducted with and without this outlier, and the results were similar.

Therefore, despite similar age, degree of obesity, and OSA severity, women reported significantly lower functional status, more subjective daytime sleepiness, higher frequency of apnea symptoms during sleep, more mood disturbance, and poorer neurobehavioral performance compared to men at baseline.

Gender Differences in Response to CPAP Treatment

The mean nightly CPAP use for all participants was 4.7 ± 2.1 hours. While the average CPAP use in women was slightly lower (4.2 ± 2.4 vs. 4.8 ± 2.1), the difference was not statistically significant (p = 0.265). One hundred (56.8% of participants [88 men and 12 women]) used CPAP ≥ 4 h per night, including similar proportions of men and women (67.7% men vs. 63.2% women, p = 0.694). In addition, 46.0% of the participants used CPAP ≥ 5 h, 28.4% for ≥ 6 h, but only 11.4% for ≥ 7 h per night. There were no significant differences between the proportions of men and women in these different durations of CPAP use.

Within each gender group, significant improvements were seen in all clinical outcomes (p < 0.05) except for the number of PVT lapses in women (p = 0.233) (Table 3). Both men and women achieved significant improvement in functional status, daytime sleepiness, mood state, apnea symptoms during sleep, and neurobehavioral performance following 3 months of CPAP treatment.

The amount of change in each clinical outcome was compared between genders (Table 3). The magnitude of change in each clinical outcome was greater in women compared to men, but none achieved statistical significance. Therefore, no significant differences in improvement of functional status, daytime sleepiness, mood, apnea symptoms, and neurobehavioral performance were observed between men and women following

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Table 1—Participant Demographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Participants n = 176</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>152 (86.4%)</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>151 (85.8%)</td>
</tr>
<tr>
<td>African American (%)</td>
<td>15 (8.5%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.7 ± 8.8</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>38.0 ± 8.2</td>
</tr>
<tr>
<td>AHI, events/hour</td>
<td>63.9 ± 29.4</td>
</tr>
</tbody>
</table>

BMI, body mass index; AHI, apnea-hypopnea index

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514
Gender Differences in Obstructive Sleep Apnea

Table 2—Comparison of Baseline Characteristics by Gender

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men</th>
<th>Women</th>
<th>Men vs Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>n</td>
</tr>
<tr>
<td>Age, years</td>
<td>149</td>
<td>46.4 ± 8.4</td>
<td>24</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>152</td>
<td>37.6 ± 8.4</td>
<td>23</td>
</tr>
<tr>
<td>AHI, events/hour</td>
<td>152</td>
<td>64.4 ± 28.9</td>
<td>24</td>
</tr>
<tr>
<td>FOSQ Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>150</td>
<td>15.0 ± 2.9</td>
<td>23</td>
</tr>
<tr>
<td>Activity level</td>
<td>150</td>
<td>2.8 ± 0.7</td>
<td>23</td>
</tr>
<tr>
<td>Vigilance</td>
<td>150</td>
<td>2.6 ± 0.8</td>
<td>23</td>
</tr>
<tr>
<td>Intimacy and sexual relationships</td>
<td>147</td>
<td>3.2 ± 0.8</td>
<td>16</td>
</tr>
<tr>
<td>General productivity</td>
<td>150</td>
<td>3.3 ± 0.6</td>
<td>23</td>
</tr>
<tr>
<td>Social outcomes</td>
<td>149</td>
<td>3.2 ± 0.8</td>
<td>23</td>
</tr>
<tr>
<td>SIP, global score</td>
<td>149</td>
<td>8.4 ± 7.7</td>
<td>24</td>
</tr>
<tr>
<td>ESS, score</td>
<td>147</td>
<td>14.5 ± 4.8</td>
<td>22</td>
</tr>
<tr>
<td>MSLT, min</td>
<td>151</td>
<td>7.0 ± 5.1</td>
<td>21</td>
</tr>
<tr>
<td>TMD, score</td>
<td>146</td>
<td>11.9 ± 25.9</td>
<td>21</td>
</tr>
<tr>
<td>MAP, apnea score</td>
<td>149</td>
<td>3.0 ± 1.0</td>
<td>24</td>
</tr>
<tr>
<td>PVT reaction time, milliseconds</td>
<td>138</td>
<td>311.1 ± 105.1</td>
<td>17</td>
</tr>
<tr>
<td>PVT number of lapses</td>
<td>138</td>
<td>4.6 ± 8.7</td>
<td>20</td>
</tr>
</tbody>
</table>

*Analyses conducted using independent-sample t tests unless indicated. †Analyses conducted using nonparametric Mann-Whitney U test. ‡t test based on reciprocal transformations. §t test based on natural logarithm transformations. △Mean ± SD with the outlier of 1828.6 milliseconds removed. FOSQ, functional outcomes of sleep questionnaire; SIP, Sickness Impact Profile; ESS, Epworth Sleepiness Scale; MSLT, multiple sleep latency test; TMD, total mood disturbance; MAP, multivariable apnea prediction; PVT, psychomotor vigilance task.

Table 3—Changes in Performance in Men and Women after CPAP Treatment

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Men vs Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Change</td>
<td>p-value*</td>
</tr>
<tr>
<td>FOSQ Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>143</td>
<td>2.9 ± 2.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Activity level</td>
<td>142</td>
<td>0.7 ± 0.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Vigilance</td>
<td>142</td>
<td>0.8 ± 0.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Intimacy and sexual relationships</td>
<td>136</td>
<td>0.4 ± 0.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>General productivity</td>
<td>142</td>
<td>0.4 ± 0.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Social outcomes</td>
<td>140</td>
<td>0.6 ± 0.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SIP, global score</td>
<td>140</td>
<td>−5.4 ± 6.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ESS, score</td>
<td>132</td>
<td>−6.5 ± 5.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MSLT, min</td>
<td>131</td>
<td>2.0 ± 4.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TMD, score</td>
<td>137</td>
<td>−14.0 ± 22.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MAP, apnea score</td>
<td>137</td>
<td>−2.8 ± 1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PVT reaction time, milliseconds</td>
<td>113</td>
<td>−8.6 (31.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PVT number of lapses</td>
<td>113</td>
<td>−0.3 (2.0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Data presented as median (interquartile Range) because they are strongly skewed. *Paired t-tests or the nonparametric Wilcoxon matched-pairs tests used to assess changes within each gender group. †t-tests or Mann-Whitney U test for comparison of the change scores between genders.

3 months of CPAP treatment. Similar results were shown in adjusted analyses using ANCOVA controlling for age, BMI, AHI, pre-treatment status and average hours of daily CPAP use (data not shown). However, when the relative change in the FOSQ Total score was calculated based on their baseline status, women showed a greater improvement in the overall functional status compared to men (38% vs 23%, p = 0.040, effect size = 0.47, natural logarithm transformations applied).

**DISCUSSION**

Using data from a multisite effectiveness study of CPAP therapy, we examined gender differences at baseline and in response to CPAP treatment in patients with severe OSA over a wide range of clinical outcomes. Despite similarities in age, degree of obesity, and OSA severity, women were found to have significantly lower functional status, more subjective daytime sleepiness, higher frequency of apnea symptoms, more mood disturbance, and poorer neurobehavioral performance at baseline. CPAP treatment significantly improved functional status and relieved OSA symptoms for both men and women. There was no significant difference between genders in response to CPAP treatment, and gender differences in CPAP adherence were not observed.

Salient gender differences were observed at baseline. Lower functional status was reported in women, detected by both disease-specific and generic measures. In a recent study that...
compared men and women with similar OSA severity, lower perceived health status and poorer functional status measured by the FOSQ were reported by women (similarly to our findings) and was hypothesized to partly explain their higher health care consumption. Our data showed that women reported significantly lower activity level and general productivity, two subscales of the FOSQ. The finding that some aspects of functional status were more impaired in women than in men with OSA is supported by a previous study of obese Swedes. In this Swedish study, women with OSA were characterized by a higher rate of impaired work performance, sick leave, and divorce compared to women without OSA. However, men with and without OSA were similar in most psychosocial variables.

OSA has been blamed for social isolation and divorce, especially in women, and women are less likely to come to clinics accompanied by their bed partners. These observations may imply a gender difference in the impact of OSA on functional status or quality of life. Further studies are needed to examine how functional status is impaired in each gender, in order to design gender-specific supports to improve quality of life.

Considering the impact of symptoms on functional status in general, specifically the correlations of functional status with daytime sleepiness and mood disturbances in OSA, the more severe symptom manifestations in women at baseline may also contribute to poorer functional status. We found a higher frequency of nocturnal apnea symptoms such as loud snoring, snorting, or gasping and apneas in women, but the converse has been reported in studies in general populations. Therefore, when interpreting the results, it should be noted that these characteristics were compared in a clinical sample including middle-aged obese men and women with more severe OSA. Greater mood disturbance in women with OSA has been reported previously, consistent with our finding. It has been argued that mood disturbance, which is an atypical symptom of OSA, may arise from basic personality characteristic differences between genders, rather than sleep apnea. In general, women report more somatic symptoms than men, which could be explained by characteristics in women such as greater bodily vigilance and awareness, more generalized psychological disturbance, as well as more social acceptance for women to express distress. We acknowledge that innate gender characteristic differences may play a role in the self-appraisal and assessment of functional status and symptoms, and consequently contribute to the observed gender differences at baseline. However, gender differences were also observed in the objective measures of neurobehavioral performance and most post-treatment scores were similar between genders, suggesting that the observed gender differences at baseline were not due solely to differences in gender specific personality characteristics. Although the observation of more impaired functional status at baseline in women may be partly caused by women’s greater mood disturbance, our additional analysis does not support a differential effect of mood on response between genders. Women still reported poorer functional status scores after controlling mood score as a covariate. To fully address this potential response bias, normal controls are needed in future investigations in gender differences in OSA clinical manifestations.

Both subjective and objective sleepiness were assessed in this study. Women reported a 2.3-point higher ESS score on average, but this difference in subjective sleepiness was not reflected in objective sleepiness measured by the MSLT. Our findings are consistent with the results from a large retrospective study that reported gender had considerably more influence on the ESS than on the MSLT. It has been suggested that the ESS measures sleep propensity in real-life situations, which may differ from physiologic sleep tendency measured by the MSLT. Therefore, it is possible that women report more sleepiness than men when they have the same level of physiologic sleepiness. The participants in this study had severe OSA with a high level of subjective sleepiness. At this high level of symptomatic severity, this 2.3-point difference between genders may not represent different level of self-assessed sleepiness. However, this difference was similar with the findings in a previous clinical study in mild to moderate OSA, in which male gender predicted a 2.2-point lower ESS score even after controlling for OSA severity and age. Other studies in large community samples also suggest the existence of more daytime sleepiness in women with OSA. For example, the prevalence of self-reported excessive daytime sleepiness was significantly higher among women than men with OSA in the Wisconsin Sleep Cohort Study, and women who snored reported more daytime sleepiness than male snorers. That a significantly higher proportion of women in our sample who reported ESS scores > 10 further suggests a higher level of subjective sleepiness in female patients. If women report more daytime sleepiness, as suggested by our analysis and other studies, it is critical to examine why current clinical practice, which emphasizes sleepiness as a feature of OSA, does not facilitate the identification of women with this disorder. One possible explanation is that women may report their sleepiness differently and have a tendency to emphasize fatigue, tiredness, or lack of energy more than sleepiness. Additional examination of gender differences in daytime sleepiness, especially in how men and women report sleepiness, will contribute to rectifying clinical underrecognition of OSA in women.

A gender-based referral bias may also contribute to our observation at baseline. Referral bias may be caused by the lack of understanding of gender differences in clinical presentation, and a low awareness of OSA in women due to the stereotype that OSA is a male disease in health care providers. As a result, only female patients with typical clinical features or more severe symptoms of OSA are likely to be referred for evaluation. The 6.3 to 1 male-to-female ratio in our sample, in contrast to only a 2–3.5 to 1 seen in the general population, suggests this referral bias. Further studies in community samples are needed to confirm our observations in this clinical sample.

CPAP treatment significantly improved impaired functional status, daytime sleepiness, mood state, apnea symptoms, and neurobehavioral performance in both men and women. These improvements confirm the effectiveness of CPAP in both men and women. A tendency toward greater improvement in each outcome was observed in women compared to men, but none of the comparisons were statistically significant. We believe that the small number of women in the sample may impede detection of a statistically significant difference in treatment response by gender. This preliminary investigation, although underpowered, may provide important preliminary data for further investigation. Ideally, to evaluate gender differences in treatment response, it would have been better to consider the placebo effect, which may be different between genders. The original multisite study was designed as an effectiveness study.
to investigate what normally occurs in routine clinical practice, and did not contain a control group. Adequately powered studies examining gender differences in response to CPAP treatment are needed, with special consideration of potential gender differences in placebo effects on subjective outcomes.

We did not find any gender difference in CPAP adherence. Similarly, in a recent published study comparing 233 pairs of age and BMI-matched male and female Finnish patients, no differences in CPAP adherence were found. In contrast, gender differences in CPAP adherence have been demonstrated in some other studies. Female gender was found to be predictive of CPAP noncompliance in one study, but was significantly correlated with increased CPAP use in another. The inconsistent relationship observed between gender and CPAP adherence might be due to different sample characteristics such as age and symptomatic severity of the participants. Lack of consistency in findings underscores the importance of further study of gender differences in CPAP use.

Gender differences in response to other treatment options for OSA have been reported. For example, given the finding that apnea severity is less weight-dependent in women than men, weight loss might be a more effective treatment strategy in men. With regard to mandibular advancement devices, women are more likely to have treatment success than men (success defined as an AHI < 10 in both the supine and lateral positions), particularly in individuals with milder OSA. However, treatment response in these studies was limited to the examination of the change in disease severity. CPAP is a unique treatment requiring consistent use every night, and therefore, it has great impact on patients’ everyday life. If gender differences in the response to CPAP exist, they are likely to be explained by multiple reasons including social-cultural factors, in addition to physiological differences. One advantage of our study is the ability to explore gender differences in response to CPAP over a wide range of outcomes (functional status, daytime sleepiness, mood, apnea symptoms, and neurobehavioral performance) that are applicable to the clinical management of OSA. Understanding gender differences in response to treatment by examining these clinical outcomes is important for potential treatment guidelines and interventions tailored to gender.

This study was conducted in a male-dominant sample, which is commonly seen in clinical reports. In addition to the gender-based clinical referral bias, other factors may have contributed to this high male-to-female ratio (6.3 to 1). OSA seems to be less severe in women with regard to the mean total number of apneic events. The fact that most of the participants (81.8%) had severe OSA may have contributed to this high ratio. In addition, patients older than 60 years were excluded. Since women with OSA are usually older than men on average, this criteria might have disproportionally excluded more women than men. As an exploratory investigation, small sample size in women may have impeded detection of statistically significant gender differences, especially in response to CPAP treatment. Multiple testing was involved in this study when examining gender differences in a wide range of clinical outcomes. Due to the small sample size in women in this exploratory study, Bonferroni correction or other statistical method was not applied to control the overall α level. Therefore, some significant findings at baseline need to be further tested in larger studies when multiple testing is taken into account. Lack of controlling for some important covariates such as menopausal status is another limitation. Because of the limited number of women in the sample, we did not stratify the data by menopausal status or menstrual cycle. Medication use was not found to differ between genders and was not controlled in this study. Concurrent medical conditions as well as medication use need to be scrutinized in future studies as they may contribute to the gender differences in clinical manifestations in patients with OSA.

This study shows significant differences between men and women in functional status, subjective sleepiness, apnea symptoms, mood disturbance, and neurobehavioral performance at baseline, adding to the growing evidence that women with OSA have different clinical manifestations. Understanding gender differences in clinical manifestations will not only contribute to greater recognition in women with OSA by the clinicians, but also help to develop gender-sensitive interventions and consultations aimed to improve quality of life in this population. Remarkably few studies have examined gender differences in therapeutic management for OSA. Our investigation showed both genders benefited from CPAP treatment. As an exploratory investigation, this study is limited to the small number of women in this clinical sample with more severe OSA. Further studies describing clinical manifestations in men and women at different levels of OSA severity will substantially contribute to the ability to identify and treat OSA in women across a wide spectrum of disease severity. Referral bias needs to be considered when examining gender differences using clinical samples. Including normal controls from non-OSA population is necessary to avoid potential response bias caused by innate gender characteristic differences. Adequately powered studies with consideration of potential gender differences in placebo effects are needed to elucidate gender differences in response to CPAP treatment. It is hoped this exploratory investigation into gender differences in OSA clinical manifestations and response to CPAP treatment will serve as a preliminary study to inspire future research in this largely unexplored area.

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