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SCIENTIFIC INVESTIGATIONS

Are there sex-related differences in therapeutic CPAP levels in adults undergoing in-laboratory titration?

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Study Objectives: The first-choice therapy for adults with moderate/severe obstructive sleep apnea is continuous positive airway pressure (CPAP). However, studies evaluating whether the therapeutic CPAP level obtained from a titration is affected by sex are surprisingly scarce. Our main objective was to verify if sex influenced the optimal CPAP measurement obtained during a titration.

Methods: This cross-sectional study was conducted in adults diagnosed with moderate/severe obstructive sleep apnea [baseline apnea-hypopnea index (AHI) ≥ 15.0 events/h] who underwent auto-adjusting CPAP titration (S9 or S10 AutoSet ResMed) in a sleep laboratory setting. All participants used a nasal mask during the titration. The optimal pressure, leak, and residual AHI values were registered. Multiple linear regression was used to evaluate if clinical and polysomnographic data influenced the therapeutic CPAP level setting (95th percentile pressure).

Results: A total of 1,006 adults were enrolled: 354 women and 652 men. There were no statistically significant sex-related differences in the CPAP requirements and leak values delineated during the titration; all *P*-values > .005. However, the median residual AHI was significantly higher in males vs females: 2.7 events/h vs 2.2 events/h ($P = .008$). Body mass index (β: 0.292, $P < .001$), baseline AHI (β: 0.167, $P < .001$), and age (β: 0.065, $P = .035$) were independent predictors of the therapeutic CPAP level settings.

Conclusions: Sex does not significantly influence the therapeutic CPAP settings. However, age, BMI, and baseline AHI emerge as independent predictors of the 95th percentile CPAP requirement during an auto-adjusting CPAP titration.

Keywords: obstructive sleep apnea, CPAP titration, pressure measurements, sex

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Sex is clearly associated with several clinical, anthropometric, and polysomnographic differences in the presentation of patients who experience obstructive sleep apnea. However, studies focusing on whether sex influences the outcomes associated with overnight continuous positive airway pressure titration are surprisingly scarce.

Study Impact: Sex did not influence the achievement of an optimal continuous positive airway pressure level. Conversely, body mass index, age, and baseline apnea-hypopnea index were all independent predictors to obtain the therapeutic level of continuous positive airway pressure from an overnight titration.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repeated episodes of total or partial closure of the upper airways during sleep leading to intermittent oxygen desaturation and sleep fragmentation and is an exceedingly common sleep-related disorder that is associated with a large number of comorbidities, notably affecting cardiovascular, metabolic, and neurocognitive systems.[1,2] Since its inception in the early 1980s, the most effective treatment of moderate/severe OSA [apnea-hypopnea index (AHI) ≥ 15.0 events/h] is predicated on the use of continuous positive airway pressure (CPAP) during sleep. CPAP maintains the patency of the upper airways during sleep and suppresses obstructive respiratory events, thereby normalizing nocturnal oxygenation and sleep architecture.[3–5] Several studies have demonstrated the benefits of adherent CPAP use on several clinical outcomes.[6–11] Although the effectiveness of CPAP treatment in correcting obstructive respiratory events is well established, many patients do not tolerate CPAP and do not adhere to the proposed treatment.[12,13] However, no significant differences have emerged regarding the benefits of CPAP between men and women.[14]

The main risk factors associated with OSA are male sex, advanced age, and obesity.[2] Of note, there are marked differences related to the clinical presentation and polysomnographic findings between men and women. Several studies reported that men are more likely to present symptoms such as loud snoring and witnessed apneas, while women usually have atypical symptoms, notably tiredness, fatigue, insomnia, and depressive symptoms.[15–17] As for polysomnographic findings, men have a higher prevalence of OSA than women, while women exhibit increased clustering of their respiratory abnormalities during rapid eye movement compared to men.[15–19]

Although there are marked clinical and polysomnographic differences between men and women with OSA, studies assessing whether sex influences the pressures derived during CPAP titration are surprisingly scarce. A previous retrospective study observed that the optimal pressures needed for CPAP treatment were significantly greater among men compared to women: 12.7 ± 3.48 cm H_2O vs 10.2 ± 2.10 cm H_2O, $P < .0001$.[20] However, several notable limitations are worthy of mention in this study, namely that: (1) there was a predominance in the sample of women over men (58.9% vs 41.1%), which is not characteristic of the general population, in which there is a clear predominance of men; (2) the AHI obtained by baseline polysomnography (PSG) was similar between sexes ($P = .13$), which is also not commonly observed, as men generally present more severe forms of OSA than women; and (3) there was no mention of which mask type (nasal or oronasal) was used during the titration, although several studies suggest that the therapeutic CPAP level is undoubtedly influenced by the type of mask used in the titration.[21–23]

In the context of the aforementioned considerations, the present study was designed to assess whether the pressure settings required for treatment were different among sexes during an auto-adjusted CPAP titration in adults diagnosed with moderate/severe OSA and exclusively evaluated with a nasal mask. In addition, we also explored whether other clinical parameters, such as age, body mass index (BMI), neck circumference (NC), and Epworth Sleepiness Scale (ESS), were independently associated with the therapeutic CPAP level.

METHODS

Ethical considerations and study design

The study protocol was approved by the Research Ethics Committee of the Federal University of Rio de Janeiro, and all participants gave written informed consent before enrollment. Anonymity was strictly preserved, and all procedures were carried out in accordance with the Helsinki Declaration. This cross-sectional study was conducted from January 2017 to December 2020. The eligibility criteria to participate were as follows: individuals aged 18 years or older, with a diagnosis of moderate/severe OSA (AHI ≥ 15.0 events/h at baseline PSG), and referred for CPAP titration performed in a sleep-lab setting. Exclusion criteria were defined as follows: (1) individuals who were already on regular CPAP treatment, (2) those for whom the baseline PSG was not available, (3) patients who underwent bilevel positive airway pressure titration, (4) those whose titration was conducted with an oronasal mask, (5) individuals who started titration with a nasal mask but switched to an oronasal mask, and (6) those who stopped the titration procedures before completion.

Clinical data acquisition

Sex, age, BMI, NC, and ESS were systematically collected by sleep technicians before performing baseline PSG. BMI was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2), while NC (in cm) was measured using a flexible tape measure with all participants seated and in an upright position. Excessive daytime sleepiness was self-reported and assessed by the ESS: scores ≥ 11 points (from 0 to 24 points) were indicative of the presence of excessive daytime sleepiness.[24]

Sleep studies

All sleep tests (baseline PSG and CPAP titration) were performed at a single center: SleepLab–Laboratório do Sono, Rio de Janeiro, Brazil. All participants underwent an attended PSG (EMBLA S7000; Embla Systems, Inc, Broomfield, CO) consisting of an overnight recording of electroencephalography, electrooculography, electromyography (chin and legs), electrocardiography, airflow, thoracic and abdominal impedance belts, arterial oxygen saturation (SpO_2), pulse rate, microphone for snoring, and body position sensors. Polysomnographic data were manually scored according to the standard criteria[25] by 2 certified sleep physicians. Polysomnographic data included AHI and SpO_2 (average and nadir) values. Obstructive apneas were defined by a decrease of at least 90% in the airflow associated with persistent respiratory effort and lasting more than 10 seconds. Hypopneas were classified by a decrease of at least 30% in airflow for at least 10 seconds, associated with ≥ 3% oxygen desaturation or arousal. The AHI was calculated as the number of apneas plus hypopneas divided by the total sleep time measured in hours, with the severity of OSA calculated on the basis of AHI thresholds: ≥ 5.0 events/h as any OSA, ≥ 15.0 events/h as moderate/severe OSA, and ≥ 30.0 events/h as severe OSA.

After, all participants diagnosed with moderate/severe OSA underwent an auto-adjusting CPAP titration (S9 or S10 AutoSet; ResMed, Sydney, Australia) with humidification in a sleep laboratory setting. All nasal masks were selected from the available commercial line manufactured by ResMed. The attending sleep technician provided instructions about the sleep titration and performed the mask fitting prior to performing the titration. The devices were programmed to apply a minimum pressure of 4.0 cm H_2O and a maximum pressure of 20.0 cm H_2O, with the relief of expiratory pressure set at 3.0 cm H_2O. Whenever necessary during titration, additional adjustments were made by the sleep technician during titration to minimize leak and maximize patient comfort. The auto-adjusting CPAP data were downloaded using the ResScan software and data associated with pressure levels (50th percentile, 95th percentile, and maximum), leak (50th percentile, 95th percentile, and maximum), and residual AHI were recorded. All the titration studies were independently reviewed by 2 board-certified sleep physicians.

Statistical analysis

Data analysis was carried out using SPSS for Windows statistical software (version 21.0; Chicago, IL). Results are summarized as the median and interquartile range (IQR) or as number and percentage for continuous and categorical variables, respectively. Comparisons between groups were evaluated using the chi-squared test for dichotomous variables and the nonparametric Mann-Whitney test for continuous variables. The multicollinearity—among the continuous variables—was excluded if the variance inflation factor < 10.0 and tolerance > 0.1. After excluding multicollinearity, multiple linear regression was used to assess the relationship between the various continuous explanatory variables and the dependent variable (95th percentile pressure), with comparisons based on the standardized regression coefficient (β). The *R*-squared (R^2; coefficient of determination) was employed as a goodness-of-fit measure for the linear regression model. All tests used were 2-tailed and the statistical significance was assumed at a *P*-value of < .05.

RESULTS

Overall, 1006 consecutive participants were allocated into 2 independent sex-related cohorts: 354 women (35.2%) and 652 men (64.8%) (**Figure 1**). As illustrated in **Table 1**, the median age was 57.0 years (IQR: 45.0–67.0) and the median BMI was 29.4 kg/m^2 (IQR: 26.6–32.8). Women were older (P < .001), had smaller NC (P < .001), and lower ESS scores (P < .001) compared to men. According to the baseline diagnostic PSG, men had a higher median AHI than women: 43.1 events/h (IQR: 29.9–60.2) vs 36.7 events/h (IQR: 26.4–51.7); P < .001; **Table 1**.

Table 2 summarizes the CPAP titration measurements in women and men. The CPAP (50th percentile, 95th percentile, and maximum) and leak (50th percentile, 95th percentile, and maximum) values were similar in men and women (all *P*-values > .005). However, the median residual AHI was significantly higher in males vs females: 2.7 events/h (IQR: 1.3–5.4) vs 2.2 events/h (IQR: 1.0–4.5); P = .008.

As can be seen in **Table 3**, there was no evidence of multicollinearity between the various variables, since all parameters showed tolerance > 0.1 and variance inflation factor < 10.0. The analysis resulted in a statistically significant model (R^2: 0.158, P < .001), whereby the BMI (β: 0.292, P < .001), baseline AHI (β: 0.167, P < .001), and age (β: 0.065, P = .035) were significant and independent predictors of the therapeutic CPAP levels obtained from in-lab titration.

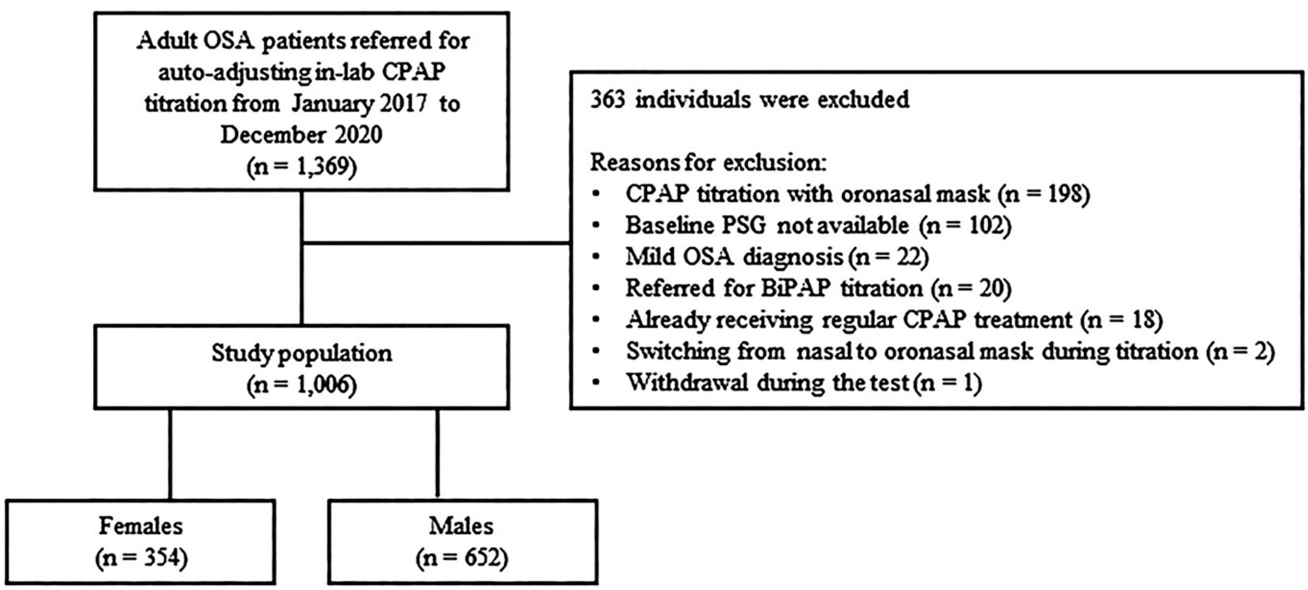
DISCUSSION

In the present study, 2 major findings deserve to be highlighted: First, the sex of the patient did not significantly influence the pressure settings for optimal CPAP therapy, nor did it affect mask leak during an in-lab titration with an auto-adjusting CPAP. Second, multiple linear regression that included relevant clinical and PSG parameters that could potentially influence CPAP requirements during auto-adjusted CPAP titration, revealed that only BMI, baseline AHI, and age were independent predictors of therapeutic CPAP settings.

Despite clear differences in the clinical and polysomnographic presentation of OSA between men and women, there were no differences in CPAP titration final settings. As indicated, all study participants underwent CPAP titration with a nasal mask, which, in light of the current evidence, should be considered as the preferential patient-machine interface choice during a CPAP titration. However, BMI, baseline AHI, and age seem to affect the correction of respiratory events during a titration study with auto-adjusted CPAP.

In a prior study developed to identify the degree of OSA severity and the excessive daytime sleepiness in Japanese adults, female patients had significantly lower optimal levels of CPAP than male patients.[26] However, the type of mask (nasal or oronasal) during the titration was not specified, and whether all participants had been diagnosed with moderate/severe OSA or if patients with mild OSA were also included was also not specifically addressed. In another study, which was designed to assess whether sex influenced the optimal CPAP settings, women emerged as needing lower CPAP pressures.[20] These findings were potentially anticipated since women typically have a lower tendency for upper airway collapse,[27,28] more negative pharyngeal critical closing pressure (P_{crit}),[29] experience less severe OSA than men (when expressed as AHI), and have apneic events

Figure 1—Patient recruitment flowchart.



BiPAP = bilevel positive airway pressure, CPAP = continuous positive airway pressure, OSA = obstructive sleep apnea, PSG = polysomnography.

Table 1—Patient characteristics.

Parameter	All Patients (n = 1,006)	Females (n = 354)	Males (n = 652)	*P*
Clinical data				
Age, years	57.0 (45.0–67.0)	63.0 (54.7–70.0)	51.0 (41.0–63.0)	< .001
BMI, kg/m^2	29.4 (26.6–32.8)	29.2 (26.4–32.4)	29.6 (26.8–33.0)	.154
NC, cm	41.0 (38.0–43.0)	37.0 (35.0–39.0)	42.0 (40.0–45.0)	< .001
ESS, points	10.0 (6.0–14.0)	9.0 (5.0–14.0)	10.0 (6.0–14.0)	.043
Baseline PSG				
AHI, events/h	40.5 (27.9–57.5)	36.7 (26.4–51.7)	43.1 (29.9–60.2)	< .001
AI, events/h	15.1 (6.0–32.7)	11.2 (4.6–23.3)	18.0 (7.4–36.9)	< .001
HI, events/h	19.8 (13.0–29.5)	22.1 (14.7–30.7)	18.7 (11.9–28.9)	.002
Average SpO_2, %	92.9 (91.3–94.0)	92.6 (91.0–93.8)	93.0 (91.6–94.0)	.019
Nadir SpO_2, %	80.0 (74.0–84.0)	80.0 (74.5–84.0)	80.0 (74.0–84.0)	.876

Data are given as median (interquartile range). The *P* value represents the comparison among sexes. AHI = apnea-hypopnea index, AI = apnea index, BMI = body mass index, HI = hypopnea index, NC = neck circumference, ESS = Epworth Sleepiness Scale, PSG = polysomnography, SpO_2 = oxygen saturation.

Table 2—CPAP requirements, leak, and residual events according to sex.

Parameter	All Patients (n = 1,006)	Females (n = 354)	Males (n = 652)	*P*
Pressure, cm H_2O				
50th percentile	7.6 (6.3–9.1)	7.5 (6.2–9.1)	7.7 (6.4–9.1)	.177
95th percentile	10.8 (9.4–12.5)	10.8 (9.3–12.4)	11.0 (9.5–12.5)	.212
Maximum	12.5 (10.7–14.6)	12.3 (10.6–14.4)	12.5 (10.8–14.6)	.195
Leak, L/min				
50th percentile	1.2 (0.0–6.0)	0.0 (0.0–6.0)	1.2 (0.0–6.0)	.874
95th percentile	12.0 (4.8–25.2)	13.2 (3.6–26.4)	12.0 (4.8–24.0)	.801
Maximum	24.0 (12.0–39.6)	24.0 (10.8–39.6)	24.0 (13.2–39.6)	.723
Residual events, events/h				
AHI	2.5 (1.2–5.2)	2.2 (1.0–4.5)	2.7 (1.3–5.4)	.008
AI	2.0 (0.9–4.4)	1.7 (0.8–3.9)	2.1 (1.0–4.5)	.086
HI	0.3 (0.1–0.6)	0.2 (0.0–0.5)	0.3 (0.1–0.7)	.001

Data given as median (interquartile range). The *P*-value represents the comparison among sexes. AHI = apnea-hypopnea index, AI = apnea index, CPAP = continuous positive airway pressure, HI = hypopnea index.

Table 3—Linear regression according to 95th percentile pressure (n = 1,006).

	β (95% CI)	*t* Test	*P*	Tolerance	VIF
Age, years	0.065 (0.001–0.022)	2.116	.035	0.894	1.118
BMI, kg/m^2	0.292 (0.107–0.174)	8.234	< .001	0.668	1.498
NC, cm	0.017 (–0.031 to 0.050)	0.465	.642	0.655	1.527
ESS, points	0.054 (–0.002 to 0.052)	1.829	.068	0.971	1.030
AHI, events/h	0.167 (0.012–0.027)	5.254	< .001	0.838	1.194
Constant	—	5.415	< .001	—	—

Collinearity was accessed by the tolerance and VIF. β represents the standardized regression coefficient. AHI = apnea-hypopnea index, BMI = body mass index, CI = confidence interval, ESS = Epworth Sleepiness Scale, NC = neck circumference, VIF = variance inflation factor. Logarithmic transformation was performed on variables with a non-normal distribution.

commonly concentrated in rapid eye movement sleep.[18,19] Therefore, it would be intuitively plausible to infer that the optimal therapeutic requirement of CPAP should be lower in women compared to men.

However, despite all these considerations, we found no differences in CPAP levels (50th percentile, 95th percentile, and maximum) between men and women. It should be highlighted that this present study included a considerably larger sample, all participants had moderate/severe OSA, and all underwent in-laboratory titration exclusively with a nasal mask, which probably increases the robustness of our findings. In light of the aforementioned studies and their limitations, and the fact that the use of oronasal masks is fraught with higher pressures,[21–23] we believe our findings are more likely to be reflective of the actual absence of differences in CPAP requirements between men and women.

Notwithstanding, hormonal effects, anatomical influences, such as craniofacial features, body/neck fat distribution, and differences in upper airway configuration can all potentially be responsible for the sex dimorphism found in clinical and polysomnographic manifestations between men and women with OSA.[30] Studies have shown that men tend to have a longer soft palate, in addition to a greater volume of soft tissues in the neck and a greater tendency to collapse of the upper airways compared to women.[30–33] A recent study reported that the thickness of the neck and waist circumference, high hypopharynx collapse, and retropalatal and retrolingual lateral wall collapse were major contributors to the need for increased therapeutic CPAP settings.[34] Conversely, no differences were reported regarding age, sex, and BMI values and the need for higher or lower CPAP pressure requirements.[34] Previous studies generally point out that anthropometric factors, such as BMI and NC, besides baseline AHI, act as predictors of optimal CPAP measurements obtained through titration.[35–39] However, it should also be stressed that patients belonging to different ethnicities may present characteristic anthropometric features that may account, at least in part, for variations in the therapeutic level of CPAP.

Although sex did not seem to affect therapeutic CPAP requirements, age, BMI, and baseline AHI were independent predictors, and significantly influenced the 95th percentile pressures during an auto-adjusting CPAP titration. These 3 variables have been repeatedly identified as significant risk factors contributing to the presence and severity of OSA[40–45] such that their inclusion in the model was not surprising.

Limitations and strengths

Our study had some limitations that must be highlighted. All participants were referred to a single sleep laboratory, which may limit the reproducibility of our findings. We did not obtain adherence measures as a follow-up to the titration procedures to examine whether some of the factors contributing to our findings influence treatment adherence. Considering that both the baseline AHI and age values were statistically different between men and women (men had higher AHI and were significantly younger than women), our data should be interpreted with caution. However, we believe that these differences may not have compromised the validity of our findings, since our study population corresponded to the prototypic type of individuals referred for CPAP titration, namely men who commonly have higher baseline AHI values than women. In addition, we should also emphasize that OSA prevalence in women increases with age, especially after menopause, such that in most clinically referred cohorts, women are generally older than men. Notwithstanding, we performed linear regression analysis that accounted for some potential confounders (ie, age, BMI, NC, ESS, and baseline AHI) but left the sex parameter in place, since sex was a categorical variable. Despite these limitations, our study included a suitable sample size of consecutively enrolled adult individuals. All participants underwent full PSG performed in our laboratory and were diagnosed with moderate/severe OSA, according to the American Academy of Sleep Medicine statement.[25] All patients were exclusively titrated with a nasal mask, which avoided the possible bias that the type of mask (nasal or oronasal) could influence the pressures obtained during a titration. Of note, all participants underwent an auto-adjusting CPAP titration, which may have negated the possibility that the titration technician's a priori expectations may have affected the optimal treatment pressures.

CONCLUSIONS

The present study, using a relatively large sample of adult individuals with moderate/severe OSA who underwent auto-adjusting CPAP titration, showed that patient sex does not influence therapeutic CPAP requirements. Conversely, BMI, age, and baseline AHI were independent predictors in the 95th percentile pressure during an in-lab titration. Future studies are needed to assess whether clinical, demographic, and anthropometric data can also influence and impact the adherence of patients during regular CPAP treatment.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
CPAP, continuous positive airway pressure
ESS, Epworth Sleepiness Scale
IQR, interquartile range
NC, neck circumference
OSA, obstructive sleep apnea
PSG, polysomnography

REFERENCES

1. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med.* 2019;7(8):687–698.
2. Patel SR. Obstructive sleep apnea. *Ann Intern Med.* 2019;171(11):ITC81–ITC96.
3. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2019;15(2):335–343.
4. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med.* 2019;15(2):301–334.
5. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet.* 1981;317(8225):862–865.
6. Peker Y, Thunström E, Glantz H, Eulenburg C. Effect of obstructive sleep apnea and CPAP Treatment on cardiovascular outcomes in acute coronary syndrome in the RICCADSA trial. *J Clin Med.* 2020;9(12):4051.
7. Martínez-Cerón E, Barquiel B, Bezos AM, et al. Effect of continuous positive airway pressure on glycemic control in patients with obstructive sleep apnea and type 2 diabetes. a randomized clinical trial. *Am J Respir Crit Care Med.* 2016;194(4):476–485.

8. Navarro-Soriano C, Torres G, Barbé F, et al; on behalf the Spanish Sleep Network. The HIPARCO-2 study: long-term effect of continuous positive airway pressure on blood pressure in patients with resistant hypertension: a multicenter prospective study. *J Hypertens.* 2021;39(2):302–309.
9. Bakker JP, Weaver TE, Parthasarathy S, Aloia MS. Adherence to CPAP: what should we be aiming for, and how can we get there? *Chest.* 2019;155(6):1272–1287.
10. Schwab RJ, Badr SM, Epstein LJ, et al; ATS Subcommittee on CPAP Adherence Tracking Systems. An official American Thoracic Society statement: continuous positive airway pressure adherence tracking systems. The optimal monitoring strategies and outcome measures in adults. *Am J Respir Crit Care Med.* 2013;188(5): 613–620.
11. Weaver TE, Maislin G, Dinges DF, et al. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep.* 2007;30(6):711–719.
12. Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. *J Otolaryngol Head Neck Surg.* 2016;45(1):43.
13. Tan B, Tan A, Chan YH, Mok Y, Wong HS, Hsu PP. Adherence to continuous positive airway pressure therapy in Singaporean patients with obstructive sleep apnea. *Am J Otolaryngol.* 2018;39(5):501–506.
14. Ye L, Pien GW, Ratcliffe SJ, Weaver TE. Gender differences in obstructive sleep apnea and treatment response to continuous positive airway pressure. *J Clin Sleep Med.* 2009;5(6):512–518.
15. Zhang Z, Cheng J, Yang W, Zou H, Su C, Miao J. Gender differences in clinical manifestations and polysomnographic findings in Chinese patients with obstructive sleep apnea. *Sleep Breath.* 2020;24(3):1019–1026.
16. Basoglu OK, Tasbakan MS. Gender differences in clinical and polysomnographic features of obstructive sleep apnea: a clinical study of 2827 patients. *Sleep Breath.* 2018;22(1):241–249.
17. Nigro CA, Dibur E, Borsini E, et al. The influence of gender on symptoms associated with obstructive sleep apnea. *Sleep Breath.* 2018;22(3):683–693.
18. Won C, Guilleminault C. Gender differences in sleep disordered breathing: implications for therapy. *Expert Rev Respir Med.* 2015;9(2):221–231.
19. Campos-Rodríguez F, Fernández-Palacín A, Reyes-Núñez N, Reina-González A. Características clínicas y polisomnográficas del síndrome de apneas durante el sueño localizado en la fase REM. [Clinical and polysomnographic features of rapid-eye-movement-specific sleep-disordered breathing.] *Arch Bronconeumol.* 2009;45 (7):330–334.
20. Jayaraman G, Majid H, Surani S, Kao C, Subramanian S. Influence of gender on continuous positive airway pressure requirements in patients with obstructive sleep apnea syndrome. *Sleep Breath.* 2011;15(4):781–784.
21. Duarte RLM, Mendes BA, Oliveira-E-Sá TS, Magalhães-da-Silveira FJ, Gozal D. Nasal versus oronasal mask in patients under auto-adjusting continuous positive airway pressure titration: a real-life study. *Eur Arch Otorhinolaryngol.* 2020;277(12): 3507–3512.
22. Genta PR, Kaminska M, Edwards BA, et al. The importance of mask selection on continuous positive airway pressure outcomes for obstructive sleep apnea. an official American Thoracic Society workshop report. *Ann Am Thorac Soc.* 2020;17(10): 1177–1185.
23. Andrade RG, Piccin VS, Nascimento JA, Viana FM, Genta PR, Lorenzi-Filho G. Impact of the type of mask on the effectiveness of and adherence to continuous positive airway pressure treatment for obstructive sleep apnea. *J Bras Pneumol.* 2014;40(6):658–668.
24. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991;14(6):540–545.
25. Berry RB, Budhiraja R, Gottlieb DJ, et al. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. *J Clin Sleep Med.* 2012;8(5):597–619.
26. Yukawa K, Inoue Y, Yagyu H, et al. Gender differences in the clinical characteristics among Japanese patients with obstructive sleep apnea syndrome. *Chest.* 2009;135 (2):337–343.
27. Mohsenin V. Effects of gender on upper airway collapsibility and severity of obstructive sleep apnea. *Sleep Med.* 2003;4(6):523–529.
28. Jordan AS, McEvoy RD, Edwards JK, et al. The influence of gender and upper airway resistance on the ventilatory response to arousal in obstructive sleep apnoea in humans. *J Physiol.* 2004;558(3):993–1004.
29. Sforza E, Petiau C, Weiss T, Thibault A, Krieger J. Pharyngeal critical pressure in patients with obstructive sleep apnea syndrome. Clinical implications. *Am J Respir Crit Care Med.* 1999;159(1):149–157.
30. Subramanian S, Jayaraman G, Majid H, Aguilar R, Surani S. Influence of gender and anthropometric measures on severity of obstructive sleep apnea. *Sleep Breath.* 2012;16(4):1091–1095.
31. Mohsenin V. Gender differences in the expression of sleep-disordered breathing : role of upper airway dimensions. *Chest.* 2001;120(5):1442–1447.
32. Segal Y, Malhotra A, Pillar G. Upper airway length may be associated with the severity of obstructive sleep apnea syndrome. *Sleep Breath.* 2008;12(4):311–316.
33. Dancey DR, Hanly PJ, Soong C, Lee B, Shepard J Jr, Hoffstein V. Gender differences in sleep apnea: the role of neck circumference. *Chest.* 2003;123(5):1544–1550.
34. Kırgezen T, Bilici S, Çakır M, Ceyran Ö, Chasan M, Yiğit Ö. Factors affecting optimal titration pressure of continuous positive airway pressure device in patients with obstructive sleep apnea syndrome. *Turk Arch Otorhinolaryngol.* 2020;58(2):80–86.
35. Choi JH, Kim EJ, Kim KW, et al. Optimal continuous positive airway pressure level in korean patients with obstructive sleep apnea syndrome. *Clin Exp Otorhinolaryngol.* 2010;3(4):207–211.
36. Loredo JS, Berry C, Nelesen RA, Dimsdale JE. Prediction of continuous positive airway pressure in obstructive sleep apnea. *Sleep Breath.* 2007;11(1):45–51.
37. Lin IF, Chuang ML, Liao YF, Chen NH, Li HY. Predicting effective continuous positive airway pressure in Taiwanese patients with obstructive sleep apnea syndrome. *J Formos Med Assoc.* 2003;102(4):215–221.
38. Oksenberg A, Arons E, Froom P. Does the severity of obstructive sleep apnea predict patients requiring high continuous positive airway pressure? *Laryngoscope.* 2006; 116(6):951–955.
39. Akahoshi T, Akashiba T, Kawahara S, et al. Predicting optimal continuous positive airway pressure in Japanese patients with obstructive sleep apnoea syndrome. *Respirology.* 2009;14(2):245–250.
40. Fietze I, Laharnar N, Obst A, et al. Prevalence and association analysis of obstructive sleep apnea with gender and age differences—results of SHIP-Trend. *J Sleep Res.* 2019;28(5):e12770.
41. Bonsignore MR, Saaresranta T, Riha RL. Sex differences in obstructive sleep apnoea. *Eur Respir Rev.* 2019;28(154):190030.
42. Horvath CM, Jossen J, Kröll D, Nett PC, Baty F, Brill AK, Ott SR. Prevalence and prediction of obstructive sleep apnea prior to bariatric surgery-gender-specific performance of four sleep questionnaires. *Obes Surg.* 2018;28(9):2720–2726.
43. Kreitinger KY, Lui MMS, Owens RL, et al. Screening for obstructive sleep apnea in a diverse bariatric surgery population. *Obesity (Silver Spring).* 2020;28(11):2028–2034.
44. Forcelini CM, Buligon CM, Costa GJK, et al. Age-dependent influence of gender on symptoms of obstructive sleep apnea in adults. *Sleep Sci.* 2019;12(3):132–137.
45. Gabbay IE, Lavie P. Age- and gender-related characteristics of obstructive sleep apnea. *Sleep Breath.* 2012;16(2):453–460.

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