



# Automatic Derivation of Continuous Positive Airway Pressure Settings: Comparison with In-Laboratory Titration

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**Background and Purpose** This study was designed to investigate differences in the final recommended pressure setting between that derived from an autotitrating continuous positive airway pressure (APAP) device and manual in-laboratory continuous positive airway pressure (CPAP) titration, as well as the factors that influence pressure differences in patients with obstructive sleep apnea (OSA).

**Methods** This study enrolled 50 patients with OSA. All patients underwent both APAP titration and manual CPAP titration. We obtained the average device pressure  $\leq 90\%$  of the time (APAP<sub>90</sub>) from the downloaded manual for the APAP machine and the optimal pressure obtained by manual CPAP titration (CPAP<sub>manual</sub>). We placed the subjects into three groups based on the pressure difference ( $\Delta P$ ) obtained by subtracting CPAP<sub>manual</sub> from APAP<sub>90</sub>: 1) Pr<sub>equal</sub> ( $\Delta P=0$ ), 2) CPAP<sub>manual+</sub> ( $\Delta P \leq -1$ ), and 3) APAP<sub>90+</sub> ( $\Delta P \geq 1$ ). Regression analysis was conducted to identify predictive factors associated with  $\Delta P$ .

**Results** The values of APAP<sub>90</sub> and CPAP<sub>manual</sub> were  $9.50 \pm 3.03$  cmH<sub>2</sub>O and  $9.48 \pm 2.71$  cmH<sub>2</sub>O (mean  $\pm$  SD), respectively ( $p=0.95$ ). The Pr<sub>equal</sub>, CPAP<sub>manual+</sub>, and APAP<sub>90+</sub> groups comprised 9 (18%), 23 (46%), and 18 (36%) subjects, respectively. Regression analyses revealed that male sex [ $\beta=3.539$ , 95% confidence interval (CI)=0.040–7.039], body mass index (BMI) ( $\beta=0.186$ , 95% CI=0.020–0.352), and average usage per day ( $\beta=0.768$ , 95% CI=0.077–1.459) were associated with  $\Delta P$ .

**Conclusions** While the mean pressure in the overall cohort did not differ significantly between APAP<sub>90</sub> and CPAP<sub>manual</sub>, there was a discordance majority showing different single pressures obtained when applying the two titration methods. Being Male, having an increased BMI, and having an increased average usage per day of APAP were significantly correlated with increased  $\Delta P$  in this study.

**Key Words** obstructive sleep apnea, polysomnography, continuous positive airway pressure.

## INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common disorder with various comorbidities such as cerebrovascular and cardiovascular disease. Various treatment options for OSAS have been suggested, but the most effective to date is positive airway pressure (PAP) treatment. The goal of PAP is to abolish manifestations of obstructive sleep apnea (OSA) in the form of apnea episodes, hypopnea episodes, arousals, oxygen saturation  $<90\%$ , and snoring in rapid eye movement (REM) sleep, in non-REM (NREM) sleep, and in the patient's habitual and most vulnerable (usually supine) body position, and to normalize the inspiratory flow contour.<sup>1</sup> Continuous PAP (CPAP) delivers a single, fixed pressure to the patient. Currently the gold-standard practice involves manual pressure titration by a sleep technologist during attended laboratory polysomnography (PSG) in order to select the acceptable pressure. However, this method of in-laboratory manual titration is labor intensive and

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**Received** November 1, 2019

**Revised** February 10, 2020

**Accepted** February 13, 2020

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costly. Moreover, the pressure requirement may change over time due to variability in body weight changes, body position changes, sleep structure changes, and underlying medical conditions.

The desire to improve the efficacy and comfort of treatment and to simplify or improve complex titration methods have led to an alternative to manual titration. Autotitrating CPAP (APAP) devices utilize an algorithm that automatically adjusts the PAP based on the patient's physiological signals, which makes pressure titration using APAP a potentially attractive alternative to manual titration for sleep physicians. Several research studies have investigated the adherence, acceptance, and functional improvement of APAP versus manual in-laboratory manual CPAP titration.<sup>2</sup> However, there has been little research into the consistency between the single selected pressure obtained by APAP titration and in-laboratory manual titration. It has been found that APAP devices may be used in an unattended manner to determine a single fixed CPAP pressure for patients with moderate-to-severe OSA without the occurrence of significant comorbidities. In the case of APAP titration in the home over several days, we generally recommend the average device pressure  $\leq 90\%$  of the time (APAP<sub>90</sub>) from the downloaded from the APAP machine (Dream Station Auto CPAP, Philips, Murrysville, PA, USA) in order to choose the single fixed pressure. The aim of this study was to characterize the agreement of the selected single pressures obtained between APAP titration at home and in-laboratory manual titration.

## METHODS

We retrospectively reviewed the medical records and PSG results of each patient who underwent PSG and was diagnosed with OSAS from May 2015 to April 2018 and who underwent overnight CPAP titration using the OmniLab Advanced device (Respironics, Murrysville, PA, USA).

All patients underwent a physical examination that included measuring the neck circumference, measuring the body mass index (BMI), and determining the social-behavior history such as alcohol consumption and smoking. We excluded patients with significant comorbidities including congestive heart disease, chronic obstructive pulmonary disease, central sleep apnea syndrome, or obesity hypoventilation syndrome. In addition, sleep questionnaires including the Epworth Sleepiness Scale (ESS),<sup>3</sup> Korean version of the Pittsburgh Sleep Quality Index (K-PSQI),<sup>4</sup> and the insomnia severity index (ISI)<sup>5</sup> were administered to all of the patients before the overnight PSG. PSG was performed using a digital PSG machine (COMET PSG and Twin 4.5.2 Software, Grass Technologies, Warwick, RI, USA).

The following variables were monitored: electroencephalogram (EEG) electrodes C3-A2, C4-A1, O2-A1, and O1-A2, right and left electro-oculograms, submental and both anterior tibialis electromyograms, electrocardiogram, airflow (using a pressure cannula and thermistor), respiratory effort (using piezoelectric bands), oxyhemoglobin saturation, and snoring. We used the 2012 American Academy of Sleep Medicine manual (version 2.0) for scoring respiratory events, which defined apnea as a decrease in the peak signal excursion by  $\geq 90\%$  of the pre-event baseline using an oronasal thermal sensor, and lasting for  $\geq 10$  seconds. Hypopnea was defined as a decrease in the nasal pressure signal to  $\geq 30\%$  of baseline that lasted for  $\geq 10$  seconds and was associated with either  $\geq 3\%$  oxygen desaturation or an arousal.<sup>6</sup>

In all participants diagnosed with moderate-to-severe OSA with an apnea hypopnea index (AHI) of 15 or more by overnight PSG, CPAP titration using the OmniLab Advanced device was manually performed in a sleep laboratory by a well-trained sleep technician following the clinical guideline for the manual titration of PAP.<sup>7</sup> The author (Yang KI) finalized the PSG data after overnight CPAP titration. Based on clinical guidelines for the manual titration for PAP in patients with OSAS, the recommended final CPAP was reached to eliminate apnea, hypopnea, flow limitation, and snoring. The results from manual CPAP titration could determine the quality of the prescribed pressure using the following grading system: optimal titration, which reduces AHI to  $< 5/\text{hr}$  for at least a 15 min and should include supine REM sleep; good titration, which reduces the overnight AHI to  $< 10/\text{hr}$  or by 50% if the baseline AHI is  $< 15/\text{hr}$  and should include supine REM sleep; and adequate titration, which does not reduce the overnight AHI to  $\leq 10/\text{hr}$  but does reduce the AHI by 75% from baseline and no occurrence of supine REM sleep.<sup>4</sup> We aimed to achieve the optimal pressure in all of the patients with OSA. The prescribed pressure was the optimal pressure obtained by manual CPAP titration (CPAP<sub>manual</sub>) when there were multiple optimal pressures as well as the oxygen saturation being at least 90%.

Before performing manual CPAP titration, all patients underwent unattended APAP titration at home using the Philips Dream Station Auto CPAP device for 10–14 nights to determine their fixed CPAP pressure. Before the onset of CPAP therapy, all patients were educated about the need to treat OSAS. How to operate the CPAP device and also the humidifier that the patients needed to use was explained to each patient, and the size of their nose was measured in order to select a nasal mask of the appropriate size. The automatic CPAP device delivered pressure from 4 to 20 cmH<sub>2</sub>O controlled by the algorithm supplied with the machine. We could obtain APAP<sub>90</sub> values from the downloaded device infor-

mation. If the result contained a number after the decimal point, the recommended pressure (which should be an integer) was rounded to the closest decimal (e.g., 13.5 cmH<sub>2</sub>O was rounded up to 14 cmH<sub>2</sub>O). Both the sleep technician and attending physician were blinded to the APAP results. We then calculated the pressure difference ( $\Delta P$ ) as APAP<sub>90</sub> minus CPAP<sub>manual</sub>.

We divided the subjects into three groups based on the calculated values: 1) when the pressure difference was less than or equal to -1 (i.e.,  $\Delta P \leq -1$ ), with CPAP<sub>manual</sub> higher than APAP<sub>90</sub> (CPAP<sub>manual+</sub>), 2) when the two pressure values were the same ( $\text{Pr}_{\text{equal}}$ ;  $\Delta P=0$ ), and 3) when the pressure difference was higher than or equal to 1 (i.e.,  $\Delta P \geq 1$ ), with APAP<sub>90</sub> higher than CPAP<sub>manual</sub> (APAP<sub>90+</sub>). The study was evaluated and approved by the Institutional Review Board at Soonchunhyang University College of Medicine, Cheonan Hospital (IRB file No. 2018-07-035).

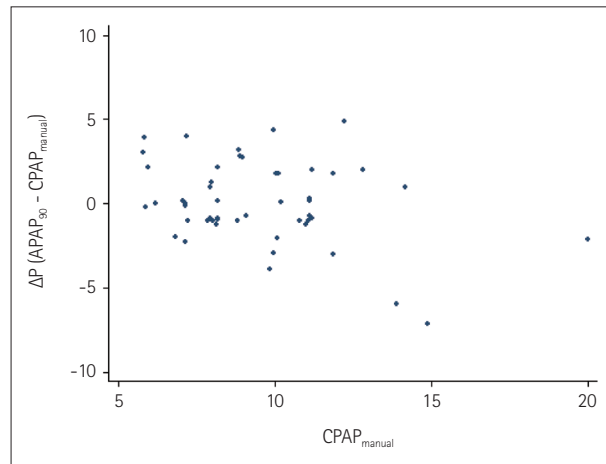
### Statistical analyses

Data are expressed as mean $\pm$ SD or *n* (%) values. The difference between the mean values of APAP<sub>90</sub> and CPAP<sub>manual</sub> was analyzed using the paired *t*-test. Unadjusted differences in continuous and categorical variables (patients' characteristics and diagnostic PSG parameters) among the three groups (CPAP<sub>manual+</sub>,  $\text{Pr}_{\text{equal}}$ , and APAP<sub>90+</sub>) were assessed for significance using analysis of variance or the chi-squared test, as appropriate. Multivariate linear regression analysis was performed to identify the predictors affecting the differences between APAP<sub>90</sub> and CPAP<sub>manual</sub>. A *p* value of less than 0.05 was considered statistically significant. All analyses were conducted using STATA (version 14.0, StataCorp, College Station, TX, USA).

## RESULTS

Fifty patients (41 males, 82%) who underwent both APAP titration at home and manual CPAP titration with laboratory PSG were enrolled. Forty-seven patients exhibited optimal titration and three patients exhibited good titration in manual CPAP titration. The APAP<sub>90</sub> and CPAP<sub>manual</sub> values were  $9.50 \pm 3.03$  cmH<sub>2</sub>O and  $9.48 \pm 2.71$  cmH<sub>2</sub>O, respectively, with no significant intergroup difference ( $p=0.95$ ). However, the pressure obtained from the two titration methods was the same ( $\text{Pr}_{\text{equal}}$ ) in only nine patients (18%) (Fig. 1), while there were 23 CPAP<sub>manual+</sub> patients and 18 APAP<sub>90+</sub> patients.  $\Delta P$  was  $1.96 \pm 1.66$  cmH<sub>2</sub>O in the CPAP<sub>manual+</sub> group and  $2.56 \pm 1.15$  cmH<sub>2</sub>O in the APAP<sub>90+</sub> group.

Table 1 lists the characteristics of the patients. There were no intergroup differences in age, sex, or BMI. The neck circumference was significantly larger, the frequency of hyper-



**Fig. 1.**  $\Delta P$  for manual CPAP titration and APAP. Most patients with obstructive sleep apnea showed a pressure difference.  $\Delta P$  was calculated as APAP<sub>90</sub> minus CPAP<sub>manual</sub>. APAP: autotitrating CPAP, APAP<sub>90</sub>: average device pressure  $\leq 90\%$  of the time, CPAP: continuous positive airway pressure, CPAP<sub>manual</sub>: optimal pressure obtained by manual CPAP titration,  $\Delta P$ : pressure difference.

tension was significantly higher, and the average usage per day was longer in APAP<sub>90</sub> than in CPAP<sub>manual+</sub>. The data on adherence to APAP therapy, usage time, and mask leakage are also summarized in Table 1.

Table 2 presents the results obtained by analyzing the diagnostic PSG parameters. Three patients were diagnosed as moderate OSA and 47 patients had severe OSA. The AHI value was highest in APAP<sub>90+</sub> ( $\text{Pr}_{\text{equal}}$ ,  $56.0 \pm 23.3$ ; CPAP<sub>manual+</sub>,  $48.7 \pm 29.5$ ; and APAP<sub>90+</sub>,  $67.4 \pm 25.0$ ;  $p=0.0995$ ), while the minimum oxygen saturation was lowest ( $\text{Pr}_{\text{equal}}$ ,  $83.1 \pm 5.4\%$ ; CPAP<sub>manual+</sub>,  $80.1 \pm 14.3\%$ ; and APAP<sub>90+</sub>,  $72.3 \pm 10.0\%$ ;  $p=0.0424$ ), as was the spontaneous arousal index (CPAP<sub>manual+</sub>,  $11.6 \pm 9.7$ ;  $\text{Pr}_{\text{equal}}$ ,  $15.3 \pm 10.2$ ; and APAP<sub>90+</sub>,  $5.4 \pm 3.8$ ;  $p=0.0097$ ). Although there were no statistically significant differences, the respiration-related and periodic limb movement (PLM)-related arousal indexes appeared to be higher in APAP<sub>90+</sub>.

Table 3 summarizes the significant factors affecting  $\Delta P$  identified in a logistic regression analysis. Male sex [ $\beta=3.539$ , 95% confidence interval (CI)=0.040–7.039], increased BMI ( $\beta=0.186$ , 95% CI=0.020–0.352), and increased average usage time per day of APAP ( $\beta=0.768$ , 95% CI=0.077–1.459) were associated with increased  $\Delta P$ .

## DISCUSSION

This study found no significant difference in the average values between APAP<sub>90</sub> and CPAP<sub>manual</sub> for the overall cohort, but there was discordance in most of the patients (82%). Previous studies similarly found no differences between APAP and manual titration pressures when comparing mean pressures.<sup>2,8</sup> However, in individual analysis, the selected single

**Table 1.** Patient characteristics in different groups of  $\Delta P$ 

Characteristic	Total (n=50)	Pr <sub>equal</sub> (n=9)	APAP <sub>90+</sub> (n=18)	CPAP <sub>manual+</sub> (n=23)	p
Age, years	49.4±11.5	49.1±10.2	46.3±12.3	51.9±11.3	0.318
Sex, male	41 (82.0)	6 (66.7)	17 (94.4)	18 (78.3)	0.170
BMI, kg/m <sup>2</sup>	29.3±5.2	26.8±5.5	31.3±4.7	28.8±5.0	0.085
Neck circumference, cm	39.8±2.9	37.6±2.2	41.6±2.6	39.3±2.6	<0.001*
Heart disease	9 (18.0)	2 (22.2)	4 (22.2)	3 (13.0)	0.702
Diabetes	6 (12.0)	1 (11.1)	2 (11.1)	3 (13.0)	0.978
Hypertension	23 (46.0)	2 (22.2)	13 (72.2)	8 (34.8)	0.017*
Hyperlipidemia	15 (30.0)	2 (22.2)	5 (27.8)	8 (34.8)	0.759
ESS score	9.88±5.60	9.78±5.04	11.67±5.90	8.52±5.39	0.863
ESS score ≥11	19 (38.0)	3 (33.3)	9 (50.0)	7 (30.4)	0.419
K-PSQI score	7.96±3.42	7.56±3.91	7.83±2.86	8.21±3.75	0.874
K-PSQI score ≥5	40 (80.0)	7 (77.8)	14 (77.8)	19 (82.6)	0.913
ISI	13.64±6.60	15.00±7.31	14.39±6.28	12.52±6.69	0.880
ISI ≥15	24 (48.0)	4 (44.4)	9 (50.0)	11 (47.8)	0.963
Smoking					0.015*
Never	13 (26.0)	4 (44.4)	2 (11.1)	7 (30.4)	
Current	29 (58.0)	2 (22.2)	11 (61.1)	16 (69.6)	
Past	8 (16.0)	3 (33.3)	5 (27.8)	0 (0)	
Alcohol consumption, %					0.655
<3 times weekly	39 (78.0)	8 (88.9)	14 (77.8)	17 (73.9)	
≥3 times weekly	11 (22.0)	1 (11.1)	4 (22.2)	6 (26.1)	
APAP summary					
Days ≥4 hr, %	64.4±25.4	70.5±25.9	65.9±23.8	60.7±26.9	0.595
Cumulative usage, hr	81.4±57.3	86.4±70.6	87.1±61.4	75.1±50.1	0.777
Average usage/day, hr	5.3±1.5	6.0±1.2	5.8±1.6	4.7±1.4	0.024*
Average leak/day, L/min	29.7±9.8	23.3±3.8	31.7±9.2	30.6±11.0	0.087
APAP <sub>90</sub> , cmH <sub>2</sub> O	9.50±3.03	8.10±2.02	11.9±2.47	8.10±2.64	0.696
CPAP <sub>manual</sub> , cmH <sub>2</sub> O	9.48±2.71	8.10±2.02	9.30±2.40	10.10±3.03	0.161
$\Delta P$ , cmH <sub>2</sub> O	0.02±1.15	0	2.56±1.15	-1.96±1.66	<0.001

Data are mean±SD or n (%) values.

\*p<0.05.

APAP: autotitrating continuous positive airway pressure, APAP<sub>90</sub>: average device pressure ≤90% of the time, APAP<sub>90+</sub>: APAP<sub>90</sub> higher than CPAP<sub>manual</sub> ( $\Delta P \geq 1$ ), BMI: body mass index, CPAP<sub>manual</sub>: optimal pressure obtained by manual continuous positive airway pressure titration, CPAP<sub>manual+</sub>: CPAP<sub>manual</sub> higher than APAP<sub>90</sub> ( $\Delta P \leq -1$ ), Pr<sub>equal</sub>: same pressure ( $\Delta P = 0$ ), ESS: Epworth Sleepiness Scale, ISI: Insomnia severity index, K-PSQI: Korean version of the Pittsburgh Sleep Quality Index,  $\Delta P$ : pressure difference.

pressures from APAP titration and manual titration showed poor agreements in most subjects, which contrasts markedly from previous comparisons of APAP and manual titration methods. To our knowledge, this is the first report of agreement between the single pressures measured using both titration methods in individual patients.

The differences between APAP titration and manual titration may come from how parameters such as apnea, hypopnea, and snoring are defined, as well as the use of different recording methods. When the patient are performing manual CPAP titration with PSG recording, the EEG and respiratory effort are recording via an elastic band around the thoracic/

abdomen, while oxygen saturation is also recorded. However, in APAP titration, pressures are automatically calculated by the algorithm of the PAP machine itself without recording the EEG, body position, respiratory effort, or oxygen saturation. The definition of the respiratory events and their detection methods vary between different manufacturers of CPAP machines.<sup>8,9</sup> All of these aspects could result in discordance of selected single pressures in APAP<sub>90</sub> and CPAP<sub>manual</sub>.

Studies with various designs have been used to compare APAP and CPAP treatments. However, few studies have compared APAP and manual CPAP methods in order to prescribe a fixed single pressure. In 46% (n=23) of the cases in the pres-

**Table 2.** Diagnostic polysomnography characteristics in groups with different  $\Delta P$  values

	Total (n=50)	Pr <sub>equal</sub> (n=9)	APAP <sub>90+</sub> (n=18)	CPAP <sub>manual+</sub> (n=23)	p
Total sleep time, min	318.5±77.3	285.5±42.2	323.0±93.3	327.0±93.4	0.368
Sleep latency, min	11.9±12.9	10.4±6.7	12.1±16.6	12.4±11.8	0.929
REM latency, min	126.4±77.6	123.1±90.5	142.2±86.8	115.3±65.4	0.550
Sleep efficiency, %	74.4±16.2	72.6±11.4	73.6±13.9	75.8±19.6	0.850
NREM sleep, %	84.9±7.9	87.1±6.6	86.4±5.3	82.8±9.6	0.214
REM sleep, %	15.1±7.9	12.9±6.6	13.6±5.3	17.2±9.6	0.214
WASO, hr	86.4±51.4	99.4±41.6	93.7±53.1	75.6±53.3	0.384
Supine sleep, %	60.9±25.1	52.5±27.2	58.7±26.3	65.8±23.2	0.367
Not-supine sleep, %	39.1±25.1	47.5±27.2	41.3±26.3	34.2±23.2	0.367
Arousal index, events/hr					
Total	60.1±32.8	64.0±28.2	65.6±23.9	54.4±40.0	0.524
Related to respiration	49.3±31.7	47.1±27.6	59.3±26.1	42.3±36.1	0.234
Related to PLM	0.8±3.6	1.6±3.6	0.9±3.6	0.5±1.2	0.558
Spontaneous	10.0±8.8	15.3±10.2	5.4±3.8	11.6±9.7	0.010*
AHI, events/hr	56.7±27.7	56.0±23.3	67.4±25.0	48.7±29.5	0.100
Apnea, events/hr	23.4±28.1	20.7±25.5	30.6±24.2	19.1±31.6	0.409
Hypopnea, events/hr	33.3±15.1	35.2±11.6	36.8±21.0	29.8±9.8	0.314
Ratio of AHI					
REM/NREM sleep	1.0±0.8	1.3±1.4	0.9±0.6	1.0±0.7	0.589
Supine/not supine	12.5±29.6	15.2±32.3	7.6±23.1	15.3±33.6	0.688
PLM index, events/hr	4.0±10.6	7.2±14.0	2.7±11.2	3.7±8.9	0.582
Oxygen saturation					
Overall, %	92.7±5.1	94.5±1.8	94.5±3.6	92.4±6.7	0.542
Minimum, %	77.8±12.2	83.1±5.4	72.3±10.0	80.1±14.3	0.042*
ODI, events/hr	34.8±24.5	27.8±18.1	44.8±22.9	29.4±26.0	0.090
Sat. <90%, min	18.0±23.1	7.4±10.3	24.3±23.5	16.8±25.1	0.217

Data are mean±SD values.

\*p<0.05.

AHI: apnea hypopnea index, APAP<sub>90+</sub>: average device pressure ≤90% of the time higher than optimal pressure obtained by manual continuous positive airway pressure titration, CPAP<sub>manual+</sub>: optimal pressure obtained by manual continuous positive airway pressure titration higher than average device pressure ≤90% of the time ( $\Delta P \leq -1$ ), NREM: non-REM, ODI: oxygen desaturation index, PLM: periodic limb movement, Pr<sub>equal</sub>: same pressure, REM: rapid eye movement, Sat: <90%, time during which oxygen saturation was <90%, WASO: wake after sleep onset,  $\Delta P$ : pressure difference.

ent study, manual CPAP titration required a higher pressure than APAP titration. In this CPAP<sub>manual+</sub> group, the usage time was significantly lower for APAP than in the other groups. Such a reduction in the usage time of APAP might result in REM sleep either not being included at all or only lasting a short time. The period of REM sleep is a deterioration factor for sleep apnea, and so when the APAP usage time is less than expected, a lower prescribed pressure could be obtained.

The acceptable pressure in manual titration should be selected to optimize AHI in different body positions and sleep stages including supine and REM sleep, and to maintain oxygen saturation at above 90%. However, the APAP<sub>90</sub> from APAP titration cannot take into consideration sleep related factors such as REM/NREM sleep stages or supine/not-supine sleep positions. Performing APAP titrations over mul-

iple nights can compensate for the limitations of unattended APAP titration without PSG recording. However, there is no guideline for how long APAP titration should be performed in order to achieve the optimal pressure. In this study we chose the single fixed pressure that was acceptable as well as ensured that oxygen saturation was ≥90% in manual CPAP titration.

An APAP machine relies on the internal pressure and a vibration sensor to determine the appropriate titration, rather than audible snoring. The airflow through the nasal mask can be monitored for subtle changes in inspiration, with the pressure adjusted accordingly.<sup>9</sup> A larger neck circumference is strongly correlated with snoring sounds as well as the severity of OSAS.<sup>10</sup> Among the present subjects, the neck circumference was larger in the APAP<sub>90+</sub> group than in the other groups, which it is assumed would increase the pressure



**Table 3.** Results of multivariate regression analysis assessing predictors of  $\Delta P$ 

	$\beta$	95% confidence interval	<i>p</i>
Age	-0.023	-0.087–0.040	0.459
Male	3.539	0.040–7.039	0.048*
BMI	0.186	0.020–0.352	0.030*
Smoking			
Current vs. never	-1.945	-4.740–0.851	0.167
Past vs. never	0.207	-2.837–3.252	0.891
Alcohol			
$\geq 3$ vs. $< 3$ times weekly	-0.269	-2.156–1.618	0.774
AHI	-0.001	-0.037–0.035	0.962
Total arousal events	0.003	-0.026–0.032	0.846
Sleep efficiency	0.035	-0.050–0.120	0.404
WASO	0.017	-0.008–0.042	0.180
K-PSQI score	-1.350	-3.183–0.483	0.144
ISI	0.415	-1.099–1.929	0.582
Days $\geq 4$ hr, %	-2.311	-6.371–1.748	0.255
Average usage/day, hr	0.768	0.077–1.459	0.031*
Average leak/day, L/min	0.023	-0.053–0.099	0.537

\**p*<0.05.AHI: apnea hypopnea index, BMI: body mass index, ISI: Insomnia severity index, K-PSQI: Korean version of the Pittsburgh Sleep Quality Index, WASO: wake after sleep onset,  $\Delta P$ : pressure difference.

in vibratory snore detection transmitted from the nasal mask due to a higher frequency of vibration in these patients. The prevalence of hypertension also was higher in APAP<sub>90+</sub>. Neck circumference was recently revealed to be a novel indicator of cardiometabolic risk.<sup>11–13</sup> A high incidence of hypertension could also be associated with increased neck circumference.

Male sex and increased BMI were significantly correlated with increased  $\Delta P$  in the present study. AHI was higher in the APAP<sub>90+</sub> group than in the other groups, although the difference was not statistically significant. Previous studies have found that obesity can affect the severity of OSA, be correlated with position-dependent OSA, and increase the incidence of wake after sleep onset (WASO) by disturbing the sleep architecture in obese patients.<sup>14</sup> Male sex, higher BMI, and central fat distribution could be associated with an increased risk of unintentional mask leakage during CPAP therapy.<sup>15</sup> Increased mask leakage is an important factor contributing to titration increases by APAP titration algorithms. In severe-OSA patients with a high BMI, the pressure of the APAP will be continuously increased by the in-built algorithm without taking into consideration the patient's underlying breakdown of the sleep architecture, deterioration related to the sleep position, and habitual awakening with respiratory events. Therefore, care is needed when using the APAP<sub>90</sub> to prescribe a single fixed pressure when the patient

has a high BMI or an increased incidence of WASO.

Arousal-based scoring for both diagnostic PSG and titration in patients with OSA were emphasized in a recent study.<sup>16</sup> Eliminating sleep fragmentation using hypoxemia is important for improving daytime sleepiness and achieving good clinical outcomes in CPAP therapy.<sup>17</sup> Considering the occurrence arousal during nighttime sleep is a significant clinical factor for determining the pressure prescribed for achieving successful and effective CPAP therapy in patients with OSA. Care is therefore needed when selecting APAP titration without consideration of arousal during sleep in OSA patients who have frequent arousal events.

This study was subject to several limitations. First, most of the enrolled patients were male, and there are sex-related affects on the relationship between neck circumference and OSAS.<sup>18</sup> This represents a limitation to generalizing the results of the present study to all sexes. Second, the number of subjects in each group was too small to apply the results to general patients receiving CPAP treatment. Further studies are therefore needed to standardize candidates who could be chosen for APAP or manual CPAP titration. Third, the patients used APAP on different dates. It was difficult to control the lifestyle of the patients in their home setting, and so further research should control the dates that patients spend in the home.

In conclusion, although there was no significant difference in the overall cohort between APAP<sub>90</sub> and CPAP<sub>manual</sub>, there was a discordance majority showing different recommended pressures obtained by applying these two methods. Male sex, increased BMI, and increased average usage per day of APAP are significantly correlated with a difference in the recommended pressure between autotitration and manual titration. These findings should be considered carefully when adopting autotitration to obtain a fixed single pressure in individual patients.

### Author Contributions

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### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

## Acknowledgements

This work was supported by a grant from Soonchunhyang University Research Fund.

**Current Knowledge/Study Rationale:** Previous studies have found no significant difference in the pressure between autotitration and manual CPAP titration in their overall cohorts. However, those studies did not perform interpersonal analysis. Therefore, to investigate interpersonal differences between two titration methods, this study was designed to compare the pressure difference between manual CPAP titration and autotitration.

**Study Impact:** This research found a discordance majority showing different recommended pressures obtained by applying autotitration and manual titration. Male sex, increased BMI, and increased average usage time per day of autotitrating CPAP were significantly correlated with the difference between the two pressures. These findings should be considered carefully when adopting autotitration with the aim of achieving a fixed CPAP pressure.

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