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ORIGINAL RESEARCH

# CPAP Titration Pressure in Split-Night, Full-Night, and Home Auto-Titration: A Prospective Comparative Analysis of Patients With Moderate to Severe Obstructive Sleep Apnea

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**Purpose:** This prospective study aimed to compare titration pressures obtained using three methods—full-night titration (FN-T), split-night titration (SN-T), and home auto-titration (HA-T)— in patients with moderate to severe obstructive sleep apnea (OSA). Additionally, factors contributing to pressure differences relative to FN-T were investigated.

**Methods:** SN-T was performed on 74 patients suspected of having OSA. Those diagnosed with moderate to severe OSA who completed SN-T underwent HA-T for 2–3 weeks. FN-T was then performed on patients who adhered to HA-T for at least 70% of prescribed nights. Ultimately, 29 patients met the inclusion criteria. Titration pressures from SN-T (SN-TP), HA-T (mean pressure [HA-TPm] and 90th percentile pressure [HA-TP90]), and FN-T (FN-TP) were compared using the Wilcoxon signed-rank test. Patients were classified into pressure disparity and non-disparity groups based on differences between FN-TP and the other methods. Logistic regression analyses were performed to identify factors associated with pressure differences. Baseline characteristics in subgroup analyses were compared using independent *t*-tests or Mann–Whitney tests for continuous variables and Fisher's exact tests for categorical variables.

**Results:** The titration pressures for SN-TP, FN-TP, HA-TP90, and HA-TPm were 8, 9, 9.6, and 8.1 cm $H_2O$, respectively. All pressures correlated significantly with FN-TP ($p < 0.05$). HA-TP90 was significantly higher than FN-TP ($p < 0.05$), while FN-TP was higher than SN-TP ($p < 0.05$), with similar trends observed at the individual level. Nasal septal deviation (odds ratio 16.63, $p = 0.018$) and high apnea-hypopnea index (odds ratio 1.06, $p = 0.027$) were identified as predictors of pressure differences.

**Conclusion:** This study is the first to directly compare multiple titration pressures to standard FN-TP in the same patients. SN-T and HA-T are reliable alternatives to FN-T in moderate to severe OSA, though predictors of significant pressure variance require careful consideration.

**Keywords:** split-night titration, auto-titration, full-night titration, pressure, obstructive sleep apnea, polysomnography

## Introduction

Obstructive sleep apnea (OSA) is a sleep disorder characterized by repetitive upper airway collapse during sleep.[1] Continuous positive airway pressure (CPAP) is the gold standard for treatment of moderate to severe OSA, effectively reducing excessive daytime sleepiness, improving sleep quality, and mitigating the risk of associated comorbidities such as cardiovascular disease and metabolic disorders.[2] As CPAP delivers a single, fixed pressure to maintain upper airway patency throughout the night, it is essential to determine the optimal pressure level before initiating treatment. Inadequate pressure titration can lead to insufficient correction of OSA, which may not only negatively affect CPAP compliance but also reduces protection against OSA-related adverse outcomes, such as cardiovascular issues and daytime sleepiness.[3] This reduction in treatment effectiveness can result in poorer overall health and a decreased quality of life, emphasizing the critical need for accurate titration to optimize patient outcomes.[4] The generally accepted standard titration technique

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is in-lab full-night manual titration (FN-T) by a sleep technologist during attended laboratory polysomnography (PSG). However, FN-T requires two separate PSGs, and is therefore costly, inconvenient, and time-consuming for patients.[5]

In-laboratory split-night titration (SN-T), which combines diagnostic PSG and CPAP titration into a single-night study, has been utilized as a more efficient and cost-effective approach since the early 1990s.[6] Khawaja et al demonstrated that split-night polysomnograms, even with just the first 2–3 hours of data, can provide a relatively accurate diagnosis of OSA, even in cases with lower AHI.[7] The American Academy of Sleep Medicine (AASM) 2017 guidelines recommend considering SN-T in clinically appropriate cases to optimize resource utilization and reduce patient burden.[8] Another alternative is using unattended home auto-titration (HA-T) systems, which employ automatic positive airway pressure (APAP) devices. This option is attractive to sleep specialists, as the device utilizes built-in algorithms to adjust airway pressure in response to real-time changes in airflow, potentially offering cost and resource savings compared to in-laboratory titration methods.[9]

Given the critical role of titration pressure in determining CPAP therapy compliance and effectiveness, researchers have sought to compare the pressures obtained through various methods to the gold standard of full-night in-laboratory titration.[10,11] Such comparisons help to assess the reliability and validity of each alternative method. However, individual factors such as OSA severity, body mass index, upper airway anatomy, and titration time may influence the optimal titration pressure, confounding the interpretation of results when comparing different patient populations. To minimize the impacts of these individual factors and provide a more precise evaluation, assessing titration pressures within the same individual offers a more controlled and rigorous approach. Nevertheless, to our knowledge, no clinical trials have directly compared the titration pressures obtained using FN-T, SN-T, and HA-T within the same patient cohort.

To address this gap in literature, we conducted a prospective study to evaluate the consistency of titration pressures among SN-T, HA-T, and FN-T in patients with moderate to severe OSA. Additionally, we investigated factors associated with pressure differences between the alternative methods and FN-T.

# Materials and Methods

## Study Population

We conducted a prospective study that included consecutive adult patients (≥18 years) referred to a single sleep center between March 2016 and January 2018 with a strong suspicion of OSA based on witnessed sleep apnea, a history of habitual snoring, and excessive daytime sleepiness. Among patients suspected of having OSA, those who were deemed likely to experience difficulties using APAP due to respiratory disorders such as severe asthma or severe chronic obstructive lung disease were excluded from the study. A total of 74 eligible patients who provided written informed consent were initially enrolled. However, only 29 patients completed the study and were included in the final analysis.

## Study Design

The study design is illustrated in Figure 1. The study followed a sequential protocol starting with SN-T, followed by unattended HA-T and in-lab FN-T, ensuring that all data were collected prospectively. All 74 patients underwent the first PSG with a plan to perform a split-night protocol. Pressure titration using a positive airway pressure (PAP) device (System One REMstar Auto, Philips Respironics, Murrysville, PA, USA) was manually performed in a sleep laboratory by a sleep technician following steps recommended by AASM guidelines.[12] Out of all patients, 46 (62.1%) successfully met the following AASM titration criteria and continued the study: (1) A moderate to severe degree of OSA during a minimum of 2 hours of recording time on diagnostic PSG, and (2) at least 3 hours available to complete CPAP titration.[8]

Following the split-night titration, 46 patients underwent unattended HA-T using the same PAP device used during in-lab titration for 2–3 weeks to determine titration pressure, and the device was then returned to the hospital at the end of the time period. Before starting therapy, all patients were educated on how to operate the PAP device and not to consume alcohol during the study period to eliminate the effects of alcohol on their sleep status and titration pressure. The same 30-minute ramp time, pressure relief mode with 2 cm $H_2O$ (expiratory pressure relief mode, which reduces air pressure on exhalation for the patient's comfort), and a nasal-type mask were applied to all patients. To establish the pressure range for the APAP machine, we initially set the device to deliver a pressure range of split-night in-lab titration pressure

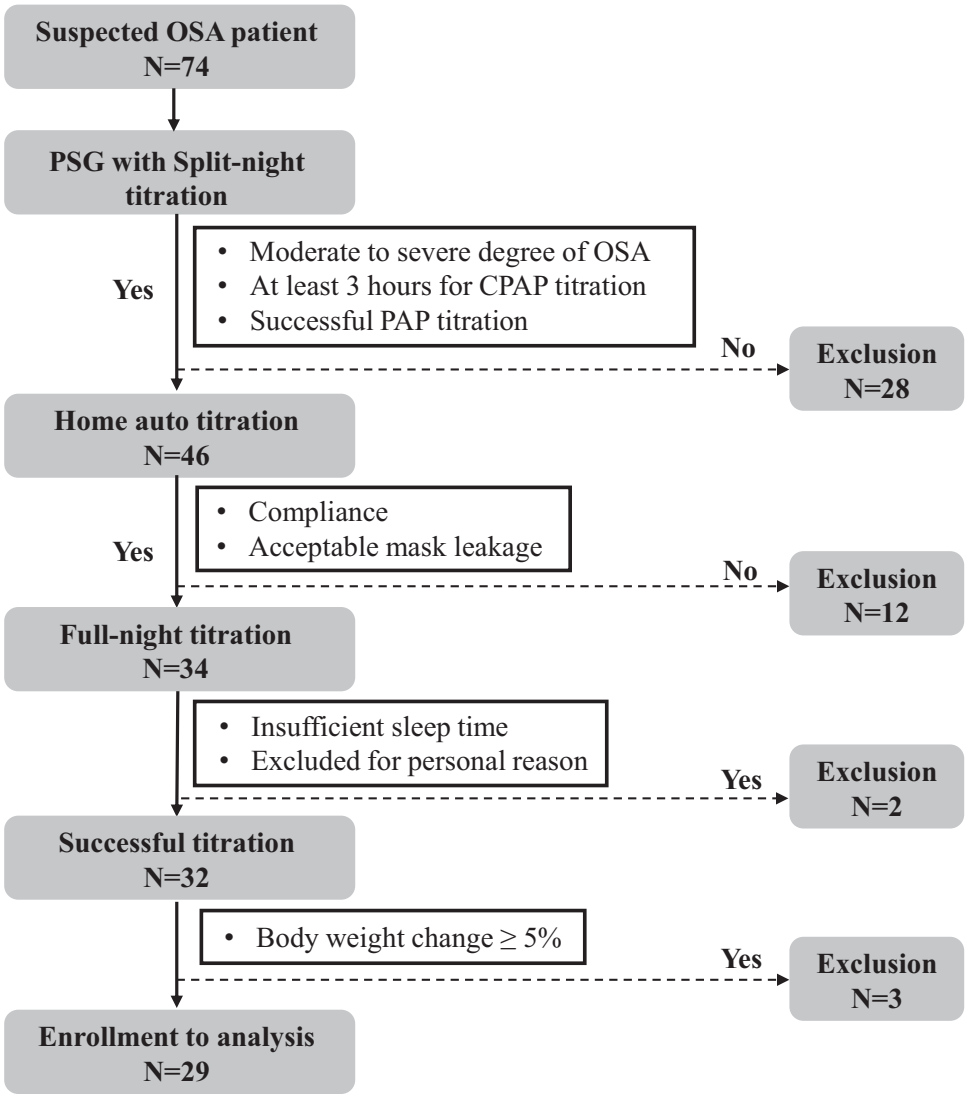


**Figure 1** Flow chart of study participants.
**Abbreviations**: OSA, obstructive sleep apnea; PSG, polysomnography; CPAP, continuous positive airway pressure; PAP, positive airway pressure.

± 4 cm $H_2O$ with a minimum pressure of 4 cm $H_2O$. Then, the pressure gradually increased or decreased to find the most appropriate pressure according to an algorithm applied by the device. After the study, the data were downloaded and reviewed for acceptability. Patients were excluded if they did not meet the compliance criteria (usage greater or equal to 4 hours per night on 70% of nights) or if mask leakage exceeded the predetermined threshold (less than 24L/min leakage in the 95th percentile).

Among the 34 eligible patients who successfully completed both split-night in-lab titration and home auto titration, 32 completed FN-T in the sleep lab administered by a sleep technologist following CPAP manual titration guidelines.[13] Two patients were excluded: one due to insufficient sleep time (less than 3 hours) for analysis during FN-T and the other for personal reasons. Additionally, three patients were excluded due to a significant change (5% or more) in body weight at FN-T, which could impact the apnea-hypopnea index (AHI) and titration pressure. Rigorous exclusion criteria were applied to ensure precise data collection, leading to 45 subjects out of 74 being excluded from the study. In total, 29 patients were ultimately included in the study analysis. All participants provided written informed consent prior to study enrollment.

This study employed a prospective observational design, wherein patient data were collected without any research-specific interventions. Consequently, the study methodology does not meet the criteria for classification as a clinical trial.


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## Sleep Studies

All PSG examinations were performed in a certified laboratory by the Korean Sleep Society in the presence of a qualified sleep physician. The following variables were recorded: sleep stages (electroencephalography and submentalis electromyography), leg movements (anterior tibialis electromyography), arousal from sleep, nasal airflow (nasal pressure transducer, thermistor), arterial oxyhemoglobin saturation (pulse oximetry), and respiratory efforts (thoracoabdominal bands). Data was recorded automatically (Embla N7000 and Remlogic version 3.2). All PSG tests were scored manually by a certified sleep technician and reviewed and interpreted by a board-certified sleep physician.

## Outcomes

The primary outcomes of this study were four titration pressure measurements obtained by three methods: SN-T (SN-TP) , FN-T (FN-TP), mean HA-T (HA-TPm), and the 90th percentile pressure of HA-T (HA-TP90). We also examined the following variables to identify factors contributing to observed pressure differences: demographic data (age, sex, body mass index, comorbidities, alcohol/smoking status, previous sleep surgery), PSG data (AHI, percentage of supine sleep position, lowest oxygen saturation level, sleep efficiency, the percentage of rapid eye movement (REM) sleep), physical examination data including nasal septal deviation (any bending of the nasal septum as shown on axial and coronal computed tomography scans or endoscopic examinations), and Friedman tonsil grade.[14]

## Statistical Analysis

The baseline characteristics of all patients are presented as medians with interquartile ranges for continuous variables and as numbers with percentages for categorical variables. Comparisons of measured pressures in the overall patient group were performed using the Wilcoxon signed-rank test.

At the individual level, Pearson's correlation test was used to analyze relationships between titration pressures. Additionally, titration pressure differences were assessed by comparing pressures obtained using three methods (SN-TP, HA-TPm, and HA-TP90) with the standard reference FN-TP. The absolute difference between FN-TP and each alternative method was calculated for each patient. Based on these differences, patients were categorized separately for each method into two groups: the pressure disparity group (absolute difference $\geq$1 cm $H_2O$) and the non-disparity group (absolute difference <1 cm $H_2O$). Consequently, three distinct disparity groups were defined: the SN-TP disparity group, the HA-TP90 disparity group, and the HA-TPm disparity group. Univariable and multivariable logistic regression analyses were performed to identify factors associated with pressure differences between the disparity and non-disparity groups. Variables with p-values < 0.10 in the univariable analysis were included in the multivariable logistic regression analysis. Logistic regression results are presented as odds ratios (OR) with 95% confidence intervals (CI).

For subgroup analyses, baseline patient characteristics were compared using independent *t*-tests or Mann–Whitney tests for continuous variables and Fisher's exact tests for categorical variables. The normality of the data was assessed using the Shapiro–Wilk test. For normally distributed data, parametric tests (independent *t*-test) were used, whereas nonparametric tests (Mann–Whitney test) were applied for non-normally distributed data. P-values < 0.05 were considered statistically significant. Statistical analyses were performed with STATA 13 (Stata Corp., College Station, TX, USA) and Prism 7 (GraphPad, San Diego, CA, USA).

# Results

## Baseline Characteristics

The study cohort consisted mainly of middle-aged, obese males, with 25 out of 29 patients displaying severe OSA. Tonsil grade 1–2 was the most prevalent, with 58.6% of patients showing nasal septal deviation. Approximately 10.3% of participants had histories of previous sleep surgery. Additional patient characteristics, such as polysomnography profiles, underlying medical conditions, and histories of smoking/alcohol consumption, are presented in Table 1.

**Table 1** Patient Characteristics

| Characteristic | Total (N = 29) |
|---|---|
| Age, years | 44.0 [40.0–55.0] |
| Sex, male | 26 (89.7) |
| Body mass index, kg/m$^2$ | 27.4 [24.7–30.1] |
| Polysomnography profile | |
| Apnea-hypopnea index, /hour | 54.7 [40.4–74.5] |
| Supine sleep, % | 95.4 [57.3–100.0] |
| Lowest $O_2$ saturation, % | 79 [71.0–83.0] |
| Sleep efficiency, % | 83.8 [72.0–88.1] |
| Rapid eye movement sleep, % | 13.9 [8.2–17.6] |
| Physical exam | |
| Nasal septal deviation | 17 (58.6) |
| Tonsil grade (0/1-2/3-4) | 3 (10.3)/24 (82.8)/2 (6.9) |
| Diabetes mellitus | 3 (10.3) |
| Hypertension | 8 (27.6) |
| Previous sleep surgery | 3 (10.3) |
| Smoking | 10 (34.5) |
| Alcohol use (times/week) | 1.0 [1.0–2.0] |

**Notes**: Data are median [interquartile range] or n (%) values.

## Comparison of Titration Pressures Measured by Each Method

Four distinct titration pressures were obtained from each patient. In the overall group, the median titration pressure and interquartile range for each method were as follows: SN-TP 8 [7–9] cm $H_2O$, FN-TP 9 [8–10] cm $H_2O$, HA-TP90 9.6 [8.3–10.8] cm $H_2O$, and HA-TPm 8.1 [7.1–9.3] cm $H_2O$. When comparing titration pressures, HA-TP90 was significantly higher than FN-TP ($p < 0.05$), while FN-TP was considerably higher than SN-TP ($p < 0.05$). However, no significant difference was observed between HA-TPm and FN-TP ($p = 0.160$) (Figure 2). For each method, the median and interquartile range of residual AHI were as follows SN-TP 1.3 [0.3–1.7], FN-TP 0.8 [0–1.5], and HA-TP 2.8 [1.8–4.8].

## Individual-Level Titration Pressure Analysis

At the individual level, the distribution of pressure data for each individual and the correlation between the four titration pressures based on each distribution are shown in Figure 3. Pearson's correlation test revealed significant positive correlations among all four titration pressures ($p < 0.001$). FN-TP exhibited the highest correlation coefficient with SN-TP ($r = 0.802$) and the lowest with HA-TPm ($r = 0.528$). In this study, pressure differences at the individual level were assessed by comparing FN-TP values with SN-TP, HA-TP90, and HA-TPm values within each participant. Based on these within-subject comparisons, participants were categorized into two groups: those exhibiting a pressure differential of 1 cm $H_2O$ or greater and those without such differences. The distribution of individuals demonstrating pressure differences was as follows: a cohort of 16 patients (55.2%) exhibited discrepancies between SN-TP and FN-TP measurements (SN-TP disparity group); a separate group of 17 patients (58.6%) displayed differences when comparing FN-TP to HA-TP90 (HA-TP90 disparity group); and, notably, a distinct assembly of 19 patients (65.5%) was identified with variances between FN-TP and HA-TPm measurements (HA-TPm disparity group) (Table 2).

In the SN-TP disparity group, the largest pressure difference was 3 cm $H_2O$ in a total of 2 patients. Individual analyses exhibited a tendency consistent with the overall group. Patients showing pressure disparities between FN-TP and SN-TP predominantly had lower SN-TP values, with one exception. In the HA-TP90 disparity group, the maximum pressure difference was 4.7 cm $H_2O$. The trend of pressure differences at the individual level was similar to the overall group, with


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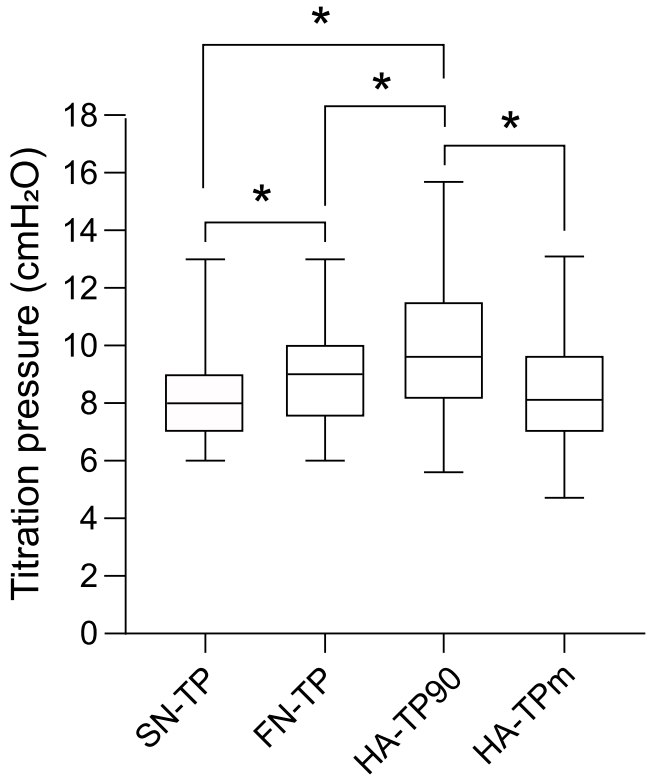


**Figure 2** Comparison of four titration pressures obtained with different titration methods in the overall group as assessed by the Wilcoxon signed-rank test (N=29). *p<0.05.
**Abbreviations**: SN-TP, split-night titration pressure; FN-TP, full-night titration pressure; HA-TP90, home auto-titration (90th percentile pressure); HA-TPm, home auto-titration (mean pressure).

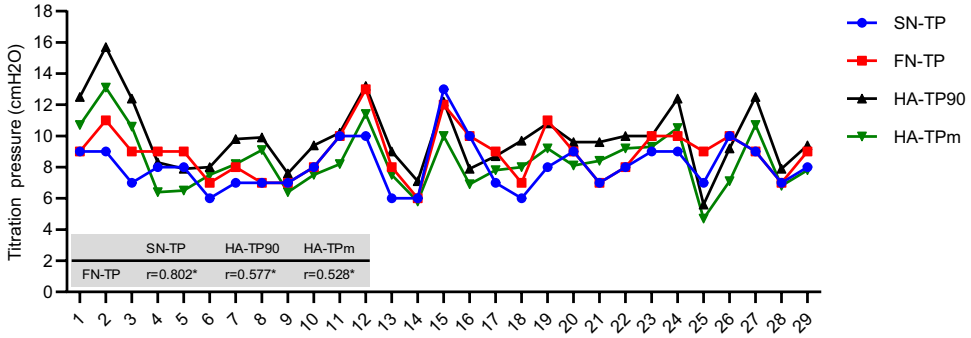


**Figure 3** Correlations between optimal titration pressures determined by different titration methods for each individual data (N=29). *p<0.05.
**Abbreviations**: SN-TP, split-night titration pressure; FN-TP, full-night titration pressure; HA-TP90, home auto-titration (90th percentile pressure); HA-TPm, home auto-titration (mean pressure).

14 out of 17 individuals having higher HA-TP90 values. However, there was a discrepancy regarding HA-TPm. Unlike the overall group, where no significant differences existed between HA-TPm and FN-TP values, the largest subset of 19 patients showed pressure disparities, with 8 having higher HA-TPm values and 11 having higher FN-TP values. The patient with the greatest pressure difference had FN-TP 4.3 cm $H_2O$ higher than HA-TPm. In the entire patient cohort, five patients had disparities in all four titration pressures, while three patients showed differences within 1 cm $H_2O$ for all four pressures.

## Predictors of Differences in Pressure Measurements

Variables associated with observed pressure differences were identified by comparing the disparity and non-disparity groups. The univariable analysis identified nasal septal deviation as a predictor of pressure differences between FN-TP

**Table 2** Patterns of Pressure Differences Within Patients Across FN-TP and Other Titration Methods

| Comparison Group (vs FN-TP) | Patients with Pressure Disparities, N (%) | Largest Pressure Difference (cm $H_2O$) | Pattern of Pressure Differences |
|---|---|---|---|
| SN-TP | 16 (55.2%) | 3.0 | Mostly SN-TP < FN-TP (15/16 patients) |
| HA-TP90 | 17 (58.6%) | 4.7 | Mostly HA-TP90>FN-TP (14/17 patients) |
| HA-TPm | 19 (65.5%) | 4.3 | Variable (HA-TPm>FN-TP 8/19 patients, FN-TP>HA-TPm 11/19 patients) |
| Patients with disparities in all three comparisons | 5 (17.2%) | - | - |
| Patients with <1 cm $H_2O$ difference in all pressures | 3 (10.3%) | - | - |

**Abbreviations**: FN-TP, full-night titration pressure; SN-TP, split-night titration pressure; HA-TP90, home auto titration pressure 90th percentile; HA-TPm, home auto titration pressure mean.

**Table 3** Factors Affecting Differences in Pressure Between Titration Methods

| | FN-TP≠SN-TP OR [95% CI] | p-value | FN-TP≠HA-TP90 OR [95% CI] | p-value | FN-TP≠HA-TPm OR [95% CI] | p-value |
|---|---|---|---|---|---|---|
| Univariable analysis | | | | | | |
| Age, years | 1.027 [0.956–1.103] | 0.463 | 1.022 [0.951–1.098] | 0.547 | 1.018 [0.945–1.097] | 0.633 |
| Body mass index, kg/$m^2$ | 0.953 [0.779–1.164] | 0.635 | 1.192 [0.940–1.512] | 0.146 | 1.238 [0.950–1.613] | 0.114 |
| Nasal septal deviation | 0.233 [0.046–1.185] | 0.079 | 6.500 [1.258–33.578] | 0.025 | 0.476 [0.094–2.418] | 0.371 |
| Smoking | 1.350 [0.286–6.379] | 0.705 | 0.583 [0.124–2.751] | 0.496 | 0.692 [0.141–3.404] | 0.651 |
| Alcohol use (times/week) | 0.973 [0.527–1.798] | 0.931 | 1.129 [0.604–2.113] | 0.703 | 0.915 [0.483–1.736] | 0.787 |
| Apnea-hypopnea index, /hour | 1.024 [0.988–1.062] | 0.197 | 1.041 [1.000–1.084] | 0.052 | 1.021 [0.983–1.060] | 0.286 |
| Lowest $O_2$ saturation, % | 0.927 [0.847–1.013] | 0.094 | 1.008 [0.939–1.081] | 0.834 | 0.929 [0.843–1.023] | 0.135 |
| Sleep efficiency, % | 0.998 [0.938–1.062] | 0.952 | 0.939 [0.870–1.013] | 0.103 | 1.027 [0.962–1.096] | 0.420 |
| Rapid eye movement sleep, % | 0.996 [0.909–1.091] | 0.928 | 0.955 [0.868–1.051] | 0.347 | 0.939 [0.847–1.042] | 0.237 |
| Supine sleep, % | 0.999 [0.978–1.021] | 0.953 | 1.007 [0.985–1.030] | 0.529 | 1.002 [0.979–1.025] | 0.891 |
| Multivariable analysis | | | | | | |
| Nasal septal deviation | 0.282 [0.052–1.537] | 0.143 | 16.634 [1.630–169.763] | 0.018 | | |
| Apnea-hypopnea index, /hour | | | 1.064 [1.007–1.125] | 0.027 | | |
| Lowest $O_2$ saturation, % | 0.927 [0.847–1.013] | 0.094 | | | | |

**Abbreviations**: FN-TP, full-night titration; SN-TP, split-night titration pressure; HA-TP90, home auto titration pressure 90th percentile; HA-TPm, home auto titration pressure mean; OR, odds ratio; CI, confidence interval.

and HA-TP90 (OR 6.500; p = 0.025) (Table 3). In multivariable analysis, nasal septal deviation (OR 16.634; p = 0.018) and higher AHI (OR 1.064; p = 0.027) were predictors of pressure differences between FN-TP and HA-TP90. No significant variables were associated with the remaining cases of pressure differences.

## Subgroup Analyses

Subgroup analyses were conducted to identify further factors contributing to pressure differences. The first analysis compared patient characteristics between those with higher HA-TPm values (n = 8) and those with higher FN-TP values (n = 11) within the HA-TPm disparity group (Table 4). Among patients with higher HA-TPm values, the proportion of nasal septal deviation was higher (87.5% vs 27.3%, p = 0.020). Although the difference was not statistically significant, AHI values were higher in the high HA-TPm group (75.8/h vs 52.7/h, p = 0.084). The second analysis compared groups with all measured pressure disparities ≥1 cm $H_2O$ (n = 5) and <1 cm $H_2O$ (n = 3) (Table 5). Despite the small sample size, the group with all measured pressure disparities ≥1 cm $H_2O$ had significantly higher AHI values (80.8/h vs 37.4/h, p = 0.016).


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**Table 4** Comparison of High HA-TPm and High FN-TP Groups in the HA-TPm Disparity Cohort

| | High HA-TPm (N = 8) | High FN-TP (N = 11) | p-value |
|---|---|---|---|
| Age, years | 44.5 [39.0–63.0] | 47.0 [33.0–65.0] | 0.908 |
| Sex, male | 7 (87.5%) | 10 (90.9%) | >0.999 |
| Body mass index, kg/m$^2$ | 29.2 [23.7–37.8] | 27.3 [22.3–32.8] | 0.134 |
| Apnea-hypopnea index, /hour | 75.8 [41.7–89.4] | 52.7 [23.2–84.6] | 0.084 |
| Supine sleep, % | 85.0 [0.0–100.0] | 94.4 [31.0–100.0] | 0.657 |
| Lowest $_2$ saturation % | 70.5 [61.0–87.0] | 79.0 [44.0–85.0] | 0.717 |
| Sleep efficiency, % | 73.9 [53.8–93.4] | 86.7 [71.1–95.2] | 0.109 |
| Rapid eye movement sleep, % | 4.7 [0.0–22.0] | 13.5 [0.0 −23.7] | 0.272 |
| Nasal septal deviation | 7 (87.5%) | 3 (27.3%) | 0.020 |
| Tonsil grade (0/1-2/3-4) | 2 (25.0)/ 5 (62.5)/ 1 (12.5) | 1 (9.1)/ 10 (90.9)/ 0 (0.0) | 0.347 |
| Diabetes mellitus | 1 (12.5%) | 2 (18.2%) | >0.999 |
| Hypertension | 5 (62.5%) | 2 (18.2%) | 0.074 |
| Previous sleep surgery | 2 (25.0%) | 1 (9.1%) | 0.546 |
| Smoking | 2 (25.0%) | 4 (36.4%) | >0.999 |
| Alcohol use (times/week) | 1.5 [0.0–4.0] | 1.0 [0.0–3.0] | 0.545 |

**Notes**: Data are presented as median [interquartile range] or number (%). Continuous variables were compared using the independent *t*-test for normally distributed variables (Age, Body mass index, Apnea-hypopnea index) and the Mann–Whitney test for non-normally distributed variables (Supine sleep, Lowest $O_2$ saturation, Sleep efficiency, Rapid eye movement sleep, Alcohol use).
**Abbreviations**: FN-TP, full-night titration pressure; HA-TPm, home auto titration pressure mean.

**Table 5** Comparison of Patients With Discrepancies in All vs Within 1 cm $H_2O$ Measured Pressures

| | All Measured Pressure Disparity ≥1 cm $H_2O$ (N=5) | All Measured Pressure Disparity <1 cm $H_2O$ (N=3) | p-value |
|---|---|---|---|
| Age, years | 44.0 [40.0–59.0] | 42.0 [33.0–43.0] | 0.143 |
| Sex, male | 5 (100.0%) | 3 (100.0%) | N/A |
| Body mass index, kg/m$^2$ | 27.4 [23.5–37.8] | 25.2 [24.6–25.7] | 0.235 |
| Apnea-hypopnea index, /hour | 80.8 [44.6–89.4] | 37.4 [33.7–42.1] | 0.016 |
| Supine sleep, % | 98.0 [0.0–100.0] | 100.0 [21.9–100.0] | 0.786 |
| Lowest $O_2$ saturation % | 71.0 [61.0–82.0] | 83.0 [80.0–83.0] | 0.071 |
| Sleep efficiency, % | 76.0 [61.0–95.2] | 83.8 [81.3–87.2] | 0.786 |
| Rapid eye movement sleep, % | 0.0 [0.0–17.6] | 15.8 [10.1–16.6] | 0.250 |
| Nasal septal deviation | 3 (60.0%) | 2 (66.7%) | >0.999 |
| Tonsil grade (0/1-2/3-4) | 2 (40.0%)/ 3 (60.0%)/ 0 (0.0%) | 0 (0.0%)/ 3 (1000%)/ 0 (0.0%) | 0.464 |
| Diabetes mellitus | 2 (40.0%) | 0 (0.0%) | 0.464 |
| Hypertension | 3 (60.0%) | 0 (0.0%) | 0.196 |
| Previous sleep surgery | 2 (40.0%) | 0 (0.0%) | 0.464 |
| Smoking | 2 (40.0%) | 2 (66.7%) | >0.999 |
| Alcohol (times/week) | 2.0 [0.0–4.0] | 2.0 [2.0–4.0] | 0.571 |

**Notes**: Data are presented as median [interquartile range] or number (%). Continuous variables were compared using the independent *t*-test for normally distributed variables (Age, Body mass index, Apnea-hypopnea index) and the Mann–Whitney test for non-normally distributed variables (Supine sleep, Lowest $O_2$ saturation, Sleep efficiency, Rapid eye movement sleep, Alcohol use).
**Abbreviation**: N/A, not available.

# Discussion

In this study, a prospective comparison of titration values obtained from four different measurement techniques was conducted with a sample of 29 patients. To our knowledge, this is the first study to compare home automatic, split-night, and full-night titration under controlled conditions in the same individuals, with a focus on comparing the first two with the standard full-night titration.

In overall participants, SN-TP was significantly lower than FN-TP, while HA-TP90 was considerably higher. Previous research by Yoshihiro Yamashiro found similar results in a group with AHI<20, suggesting that lower AHI may allow

more time for diagnosis but less for titration, leading to insufficient pressure level settings.[15] However, even in groups with AHI between 20 and 40 and above 40, SN-TP remained lower than FN-TP, though the differences were not statistically significant.

Conversely, HA-TP90 was higher than FN-TP. A previous study has also found that the 90th percentile pressure during automatic titration exceeds that of manual titration.[16] This suggests that automatic CPAP devices adjust pressure based on airflow limitations, snoring, and apnea/hypopnea events, requiring higher pressures at specific moments. In contrast, manual titration may be less responsive to these events. Additionally, air leaks, which are often caused by mask issues or mouth breathing, are significant factors contributing to higher pressures in automatic settings. Although patients with significant mask leaks were excluded from this study, automatic device responsiveness to immediate events likely led to higher 90th percentile pressures. HA-TPm showed no significant difference from FN-TP in the overall group. The mean pressure reflects the average pressure over time. Although automatic titration adjusts to higher pressures during specific events, it generally maintains lower pressures. As a result, the mean pressure in automatic titration may not differ significantly from that of full-night manual titration. These differences imply the potential variability in pressure values depending on the titration methods.

At the individual level, SN-TP, HA-TP90, HA-TPm, and FN-TP values from the same individuals were analyzed. The comparison focused on differences between the alternative pressure values and the standard FN-TP method. Any observed differences were then investigated to identify the factors associated with them.

Sixteen patients (55.2%) showed significant differences between SN-TP and FN-TP, with SN-TP generally lower, except in one case. Time constraints during split-night titration could limit the evaluation of diverse sleep states, potentially contributing to these differences.[15] A previous study has also suggested that fewer REM sleep episodes during split-night titration may contribute to discrepancies between SN-TP and FN-TP, which impair upper airway function and increase AHI.[17]

HA-TP90 showed pressure differences in 17 patients (58.6%), with HA-TP90 generally higher than FN-TP. As noted in the group comparison, the similar results in individuals are likely due to the sensitive responsiveness of automatic devices. HA-TPm showed pressure differences in 19 patients (65.5%), the highest rate of individual discrepancies. Eight participants had higher HA-TPm, while 11 had lower HA-TPm compared to FN-TP, which may have contributed to the lack of significant differences in the overall group. A subgroup analysis was conducted to investigate this variation further.

Furthermore, a correlation analysis evaluated the relationships between the pressure measurement methods. Comparison with FN-TP revealed that SN-TP had the highest correlation, likely due to both being measured in controlled laboratory settings. In contrast, HA-TP90 and HA-TPm demonstrated lower correlations, potentially reflecting pressure variability influenced by individual sleep conditions.

Next, a logistic regression analysis was performed to identify factors associated with pressure discrepancies between FN-T and other methods. Septal deviation and AHI were found to be significant factors associated with pressure discrepancies between FN-TP and HA-TP90. Miljeteig et al and Lai et al highlighted AHI as a major factor influencing variability in CPAP pressure, supporting the association observed in this study.[18,19] Additionally, septal deviation, which affects nasal airflow, has been shown to influence optimal CPAP pressure. Elwany et al conducted septoplasty or turbinate surgery on 49 patients with severe OSA and surgically correctable nasal obstruction intolerant to CPAP, observing a significant reduction in optimal CPAP pressure post-surgery.[20] Consistent findings from other studies have reported significant postoperative reductions in optimal CPAP pressure.[21–24] Septal deviation, which can impair nasal airflow and upper airway function, may similarly contribute to the pressure differences observed between FN-TP and HA-TP90.

An additional subgroup analysis was conducted to compare patients with higher HA-TPm (n = 8) and higher FN-TP (n = 11) in the HA-TPm disparity group. Significant difference was observed only in the presence of septal deviation. Among patients with higher HA-TPm, seven (87.5%) had septal deviation, compared to only three (27.3%) in the lower HA-TPm group. This suggests that septal deviation, which affects airflow, contributes to the pressure difference observed in the HA-TPm, similar to HA-TP90 disparity group. Although AHI was higher and $O_2$ saturation was lower in the high HA-TPm group, these differences were not statistically significant. These findings are likely due to the sensitivity of

automatic titration to variations in airflow and other physiologic factors, which leads to higher pressure adjustments in response to these changes.

Additionally, patients with all measured pressure disparities ≥1 cm $H_2O$ (n = 5, 17.2%) were compared to those without (n = 3, 10.3%). The group with pressure differences had significantly higher AHI, and although the difference was not statistically significant, lower $O_2$ saturation and sleep efficiency. High AHI value was a consistent factor among patients with pressure discrepancies.

In summary, individual-level analyses identified discrepancies between FN-TP and other titration methods, with elevated AHI and the presence of septal deviation emerging as significant factors associated with pressure variability. Despite these discrepancies, the strong correlations between FN-TP and alternative methods indicate their overall reliability for clinical application.

This study has several limitations. First, the sample only included Korean patients, which may limit the generalizability of our findings to individuals from other ethnic backgrounds. Second, this study included moderate to severe OSA patients eligible for APAP. Therefore, our findings may not apply to those with milder AHI requiring PAP therapy or those with contraindications to APAP.

Third, several variables that could influence titration pressure were not fully considered, including night-to-night variability in OSA severity, time lags between titration nights, body position, temporary airflow obstructions such as allergies, and mask leakage. Night-to-night variability may lead to inconsistent titration pressures due to fluctuations in sleep architecture or environmental factors. To mitigate this, patients were instructed to avoid alcohol during the APAP study period, though variability may still exist. Time lags could cause physiological or behavioral changes, such as alterations in sleep patterns or body weight. To minimize this, patients who experienced body weight change of more than a 5% change were excluded. Body position, particularly the supine position, can worsen OSA and may have influenced the results, although it was not accounted for during titration.[25] Temporary airflow obstructions, such as nasal congestion or allergies, were also not considered in the pressure comparison. Mask leakage, which may distort pressure measurements, was minimized by excluding patients with leaks exceeding a predefined threshold.[26] Additionally, nasal septal deviation may increase CPAP pressures by obstructing nasal airflow, while other factors, such as turbinate hypertrophy and sinus pathology, can also affect airflow and contribute to pressure discrepancies. These factors were not addressed in this study, and further research is needed to investigate their impact on nasal airflow and titration pressures.

Fourth, the differences between laboratories and home environments may influence study outcomes. Laboratory settings provide highly controlled conditions that minimize variability but may not accurately reflect a patient's habitual sleep patterns, as unfamiliar surroundings can disrupt normal sleep behavior. In contrast, home environments, while less controlled, offer real-world conditions that better represent natural sleep patterns and treatment responses. To reduce variability in automatic titration values in the home setting, we calculated the mean auto-titration value using data collected over a 2–3-week period. However, differences in measurement outcomes between settings may persist.

Finally, the number of participants who underwent all treatments was lower than expected (n=29), reducing the generalizability and statistical power of the study. While our study began with 74 participants, the implementation of rigorous inclusion criteria throughout each study phase, aimed at minimizing research bias, resulted in a reduced final sample size. With a small sample size, the effects of various factors influencing titration pressure may be exaggerated or underestimated, introducing potential limitations. The small sample size was due to the requirement for patients to meet all criteria for consecutive titration methods and the exclusion of cases with factors that could influence the results, such as significant weight changes. The time-consuming nature of FN-T and increased demand for PSG since mid-2018, when it was included in South Korea's national insurance coverage, led to delays of up to six months from the initial study date in some cases. However, this study is noteworthy for prospectively obtaining all four types of pressure measurements from each participant and comparing them to the standard FN-TP to evaluate discrepancies and identify associated factors. Studies with larger numbers of patients may be able to address these limitations.

## Conclusion

This study compared four pressure values obtained from three different titration methods, using FN-TP as the reference standard. HA-TP90, SN-TP, and HA-TPm showed moderate to high correlations with FN-TP, supporting their reliability as alternative titration methods in moderate to severe OSA. HA-TP90 was typically higher, and SN-TP was lower than FN-TP, which was consistent at the individual level. HA-TPm demonstrated a balanced variation, with pressures both above and below FN-TP. Discrepancies were more prominent in patients with elevated AHI or septal deviation, suggesting these factors influence pressure differences, warranting caution in obtaining titration pressures for such individuals.

## Data Sharing Statement

The datasets produced and/or analyzed during this study are not available for public access due to the policy of the Institutional Review Board of our center. However, they can be made available by the corresponding author upon reasonable request.

## Ethics Statement

Informed consent was obtained from all study participants before the start of the study. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of Samsung Changwon Hospital (IRB No. 2015-SCMC-035-00).

## Author Contributions

All authors made significant contributions to the work reported, including the conception, study design, execution, acquisition of data, analysis, and interpretation. All authors took part in drafting, revising, and critically reviewing the article, gave final approval of the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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