https://doi.org/10.5664/jcsm.9316

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Titration studies overestimate continuous positive airway pressure requirements in uncomplicated obstructive sleep apnea

Olabimpe S. Fashanu, MD, MPH[1]; Rohit Budhiraja, MD[1]; Salma Batool-Anwar, MD, MPH[1]; Stuart F. Quan, MD[1,2]

[1]Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]Asthma and Airways Research Center, University of Arizona College of Medicine, Tucson, Arizona

Study Objectives: Attended manual continuous positive airway pressure (CPAP) titration is the standard practice for determining optimal positive airway pressures for obstructive sleep apnea (OSA) treatment. However, an unattended single night auto-titrating positive airway pressure (APAP) titration is an alternative. The goal of this study was to determine whether therapeutic CPAP pressures determined during manual titrations are higher than APAP-generated surrogate pressures.
Methods: We conducted a retrospective review of 165 adults with uncomplicated OSA who had full/split-night manual CPAP titrations prior to commencing treatment with APAP. Demographic and clinical data including 30-day APAP compliance data were obtained. We compared the recommended CPAP pressure from manual titrations with the 90th/95th percentile pressure generated from APAP usage over 30 days.
Results: The recommended CPAP pressures during the manual titrations were higher than the 90th/95th percentile pressures generated from APAP (11.4 ± 3.4 vs 10.3 ± 2.4 cmH2O; $P = .000$). Almost half the group (41.9%) had their manually derived titration pressure at least 1.5 cm above the 90th/95th percentile pressure. In multivariate analyses, body mass index was the only variable that predicted higher manual titration pressures. Notably, the average residual apnea-hypopnea index on 30-day APAP data was less than the average residual apnea-hypopnea index observed at the recommended pressure during the manual titration (5.0 ± 4.3 vs 7.2 ± 8.5; $P = .006$).
Conclusions: Manual CPAP titrations may overestimate pressure requirements, particularly in patients with higher body mass index, and may not be necessary in managing patients with uncomplicated OSA. APAP appears to be at least as effective as single-pressure CPAP, while delivering lower positive airway pressure.
Keywords: auto-titrating positive airway pressure, CPAP titration, 90th percentile pressure, 95th percentile pressure
Citation: Fashanu OS, Budhiraja R, Batool-Anwar S, Quan SF. Titration studies overestimate continuous positive airway pressure requirements in uncomplicated obstructive sleep apnea. *J Clin Sleep Med*. 2021;17(9):1859–1863.

BRIEF SUMMARY
Current Knowledge/Study Rationale: Attended manual continuous positive airway pressure (CPAP) titration is the standard of care for determining pressure requirements for CPAP therapy in patients with obstructive sleep apnea. The use of 90th/95th percentile pressures obtained during unattended automatic titrations is an acceptable alternative. This study was done to determine if manually and automatically derived therapeutic positive airway pressures are equivalent.
Study Impact: The findings of this study demonstrated that manual titrations overestimate therapeutic CPAP pressure requirements. Study participants were adequately treated with lower pressures using APAP while yielding comparable reductions in AHI to those observed during titration studies. Routine manual CPAP titrations may therefore not be a necessary step in the management of uncomplicated OSA.

INTRODUCTION

Continuous positive airway pressure (CPAP) is the gold standard in the treatment of obstructive sleep apnea (OSA).[1] CPAP therapy is usually delivered via an auto-titrating or fixed-pressure mode. Manual CPAP titration during an attended polysomnographic study remains the standard of practice for determining the optimal positive airway pressure (PAP) for treatment of OSA when using fixed-pressure CPAP per the practice guidelines of the American Academy of Sleep Medicine.[2] However, a pressure obtained from an unattended single-night auto-titrating PAP (APAP) titration is an acceptable alternative.[3] Manual titrations are typically performed via full-night or split-night protocols. Nevertheless, in recent years, prescription for APAP without a prior manual CPAP titration has been recommended[1] and is being used more frequently as treatment for uncomplicated OSA.

When fixed-pressure CPAP is used, the prescribed pressure is usually determined from titration studies and less commonly from unattended APAP titrations. In contrast, when APAP is prescribed, a pressure range is specified within which the PAP adjusts to reduce obstructive events. The pressure at or below which the APAP device spends 90% or 95% (90th or 95th percentile) of usage is recognized as a surrogate measure of CPAP pressure requirements; it frequently is the pressure chosen if a patient is converted subsequently from APAP to fixed-pressure CPAP therapy.

Poor PAP therapy adherence remains a common problem encountered in the treatment of patients with OSA.[4,5] One of the major contributors toward PAP nonadherence is pressure discomfort.[6] Higher than necessary PAP pressures may indirectly contribute to low adherence via pressure discomfort, dryness, and desiccation of oronasal passages and may also contribute to the development of treatment-emergent central sleep apnea in

predisposed individuals.[7] The goal of this study was to determine whether therapeutic CPAP pressures determined during manual CPAP titration studies are equivalent to the 90th or 95 percentile pressures (P_{90-95}) obtained after treatment with APAP for at least 1 month. We hypothesized that the pressure recommendations (P_{TIT}) determined from manual CPAP titration are higher than the P_{90-95} automatically generated from 30-day APAP compliance data.

METHODS

Data were reviewed retrospectively on all adult patients (aged ≥ 18 years) with OSA who had full- or split-night manual CPAP titration polysomnograms done at the Brigham and Women's Faulkner Hospital Sleep Laboratory between September 2015 and September 2018. To be included in the study, patients were required to have been initially treated with APAP and not fixed-pressure CPAP, and to have been followed up in the sleep clinic within 18 months of the titration study. Patients who had comorbid sleep-related breathing disorders, including central sleep apnea, sleep-related hypoxemia, or hypoventilation, were excluded. Those who had been prescribed APAP with very narrow ranges (defined as maximum PAP − minimum PAP < 4 cm) and those whose minimum PAP pressure was set < 2 cm below, the same as, or > P_{TIT} were also excluded. These patients were excluded because their P_{90-95} would not reflect a sufficient variation in PAP pressures to generate an accurate P_{90-95}. A total of 922 charts were reviewed, with 165 fulfilling criteria for this study. Demographic and clinical data including 30-day APAP compliance data were collected on eligible study participants.

Statistical analysis

Baseline characteristics of study participants were summarized as means and standard deviations for continuous and interval variables and as percentages for categorical variables. Continuous variables were compared using the paired- or unpaired-sample *t* test. Categorical variables were compared using the chi-squared test. Multivariate linear regression analysis was carried out to assess the impact of relevant covariates with the observed pressure differences between P_{TIT} and P_{90-95}. Statistical tests were performed using Stata/SE (version 11.0; StataCorp, College Station, TX) and GNU PSPP 1.4.1. Free Software Foundation, Boston, MA. A *P* value ≤ .05, 2-tailed, was considered statistically significant.

RESULTS

Table 1 shows the baseline characteristics of the 165 study participants. Two manufacturers' devices were prescribed (Philips Respironics, Murrysville, PA; n = 149; ResMed, San Diego, CA; n = 16) The group comprised 119 patients (72.1%) who were prescribed APAP with a full PAP range (defined as minimum PAP of 4 or 5 and maximum PAP of ≥ 15 cm) and 46 (27.9%) who were prescribed a narrower range of PAP but with minimum PAP set ≥ 2 cm below P_{TIT}. They were majority male, middle to older aged, obese, and largely had severe OSA. Most had a split-night CPAP titration polysomnogram (70.3%).

Table 1—Baseline characteristics of study participants.

	Values
Age, y	63.2 ± 13.6
Sex, % male	54.5
Race, % non-Hispanic White	63.6
Weight, pounds	217.0 ± 53.3
Weight, kilograms	98.43 ± 24.2
BMI, kg/m^2	34.9 ± 8.4
AHI, events/hour	49.9 ± 30.1
Mild OSA, %	9.8
Moderate OSA, %	17.2
Severe OSA, %	73.0
Full-night titrations, %	29.7
Split-night titrations, %	70.3

n = 165. Values are means ± SDs unless otherwise indicated. AHI = apnea-hypopnea index, BMI = body mass index, OSA = obstructive sleep apnea, SD = standard deviation.

Treatment data are displayed in **Table 2**. No differences were observed in treatment outcomes between device manufacturers. Therefore, data were combined for all analyses. Overall, 84.2% of all the manual CPAP titration polysomnograms (split and full night) yielded a CPAP pressure recommendation that was deemed to be adequate by the reporting provider. The average clinic follow-up interval after the titration study was 5.3 ± 3.4 months. Study participants' weights remained stable at follow-up, with no significant change in weight from the time of the titration study (215.8 ± 52.5 vs 216.9 ± 53.5 pounds; 97.9 ± 23.8 vs 98.4 ± 24.3 kilograms; *P* = .21). Compliance with PAP therapy was good (mean use: 5.3 ± 2.5 hours). Notably, the average residual apnea-hypopnea index (AHI) on APAP obtained from 30-day APAP compliance data was less than the average residual AHI observed at P_{TIT} during the manual CPAP titration (5.0 ± 4.3 vs 7.2 ± 8.5 events/hour; *P* = .006). Residual AHIs < 10 events/hour and < 5 events/hour were obtained in 85.5% and 60% of

Table 2—Treatment data of study participants.

	Values
Single CPAP pressure recommended, %	84.2
Full range APAP prescribed, %	72.1
Average follow-up interval, mo	5.3 ± 3.4
Average nightly use of APAP, hour	5.3 ± 2.5
Average residual AHI, events/hour	5.5 ± 4.6
Residual AHI < 10 events/hour on APAP, %	85.5
Residual AHI < 5 events/hour on APAP, %	60.0

n = 165. Values are means ± SDs unless otherwise indicated. AHI = apnea-hypopnea index, APAP = auto-titrating positive airway pressure, CPAP = continuous positive airway pressure, SD = standard deviation.

Table 3—Comparison of titration pressure (P_{TIT}) vs 90th and 95th percentile pressure (P_{90-95}).

	Titration Recommended Pressure (P_{TIT}) (cmH2O)	90/95th Percentile Pressure (P_{90-95}) (cmH2O)	*P*
All, n = 129	11.4 ± 3.4	10.3 ± 2.4	.000
Males, n = 70	11.2 ± 3.6	10.2 ± 2.2	.010
Females, n = 59	11.7 ± 3.1	10.4 ± 2.6	.001
Age < 60 y, n = 43	11.1 ± 3.3	10.2 ± 2.5	.033
Age 60–70 y, n = 44	11.4 ± 3.1	10.3 ± 2.5	.028
Ages > 70 y, n = 42	11.8 ± 3.7	10.3 ± 2.3	.007
BMI < 30 kg/m^2, n = 33	10.6 ± 3.9	10.1 ± 2.3	.402
BMI 30–34.9 kg/m^2, n = 39	11.1 ± 2.9	10.4 ± 2.5	.179
BMI ≥ 35 kg/m^2, n = 56	12.3 ± 3.1	10.3 ± 2.5	.000
Supine REM sleep observed, n = 62	11.1 ± 3.4	9.9 ± 2.5	.004
Supine REM sleep not observed, n = 55	11.5 ± 3.3	10.6 ± 2.3	.036
Full-night titrations, n = 37	11.8 ± 3.8	10.4 ± 2.8	.020
Split-night titrations, n = 92	11.3 ± 3.2	10.2 ± 2.3	.001
Mild OSA, n = 12	9.3 ± 2.7	8.8 ± 2.1	.561
Moderate OSA, n = 21	11.4 ± 2.5	10.7 ± 2.6	.259
Severe OSA, n = 95	11.7 ± 3.5	10.4 ± 2.4	.000

Values are means ± SDs. BMI = body mass index, OSA = obstructive sleep apnea, REM = rapid eye movement, SD = standard deviation.

patients, respectively. Patients were observed at P_{TIT} for an average of 68.9 ± 65.3 minutes (range: 1.5 to 342 minutes) during the titration studies.

Only 129 of the 165 participants had complete APAP data for analysis. As shown in **Table 3**, P_{TIT} was found to be higher than P_{90-95} (11.4 ± 3.4 vs 10.3 ± 2.4 cmH2O; P = .000). Almost half of the group (41.9%) had P_{TIT} at least 1.5 cm above the P_{90-95}. Results were not different between device manufacturers. This finding persisted after stratification for sex, age, and whether supine rapid eye movement sleep was observed during the manual CPAP titration. However, for body mass index (BMI) and OSA severity, it was only significant for the most severe. In multivariate analyses, BMI was the only variable that predicted a higher P_{TIT}.

DISCUSSION

In this study, we found that mean pressure recommendations from manual CPAP titration polysomnograms were higher than the mean 90th/95th percentile pressures generated from 30- day APAP compliance data in patients with OSA. Furthermore, those with a higher BMI were more likely to have higher average P_{TIT} relative to P_{90-95}. Additionally, the residual AHI on APAP was lower than the residual AHI observed at the P_{TIT} during manual titration polysomnograms.

The primary finding from our study was that PAP requirement surrogates generated from APAP data were lower in our study population when compared with those generated during preceding manual CPAP titration polysomnograms. This agrees with most, but not all, prior studies, which have shown that optimal CPAP pressure requirements generated using APAP are lower than those obtained during manual titration polysomnograms.[8–10] In contrast, however, Kim et al[11] observed no overall difference between mean P_{90-95} and mean P_{TIT} but instead documented significant individual discordance between manually generated (P_{TIT}) and automatically generated (P_{90-95}) pressures in the majority of the study population. However, this study by Kim et al had a smaller number of participants and predominantly enrolled males. Another study showed that the 95th percentile APAP pressure was higher than P_{TIT}[12] but there were significant mask leaks in the APAP group.

Treatment pressure has been identified as an important determinant of CPAP compliance,[13] and higher CPAP pressures have been associated with poor CPAP compliance.[14] Inadequate compliance is the principal limitation with the use of CPAP in the management of OSA.[4,5] Pressure discomfort, aerophagia, and bloating are some of the many reasons that patients cite for CPAP intolerance and these can be consequences of high-pressure settings. Hence, higher prescribed CPAP pressures based on manual titration recommendations may contribute to poor compliance to CPAP therapy. Furthermore, treatment-emergent central sleep apnea also has been associated with high CPAP pressures.[7] It is thus reasonable to infer that treatment modalities like APAP, which have been shown to be effective while reducing PAP delivery, may improve compliance, although this has not been demonstrated in prior studies.[15,16] Clinically, reductions in CPAP pressure by as little as 1–2 cm can make a difference in a patient's ability to tolerate therapy. In this study, > 40% of the study participants had their P_{TIT} at least 1.5 cm above their P_{90-95}, and this would typically result in their CPAP pressure being set 1–2 cm higher if being treated with a single fixed-pressure CPAP. We acknowledge that some patients did not

achieve an AHI < 5 events/hour with the use of APAP and may have had residual symptoms such as daytime sleepiness. However, failure to achieve an AHI < 5 events/hour is common, even with ongoing use of fixed-pressure CPAP.[17,18] Inasmuch as it is unclear whether mild OSA is associated with excess cardiovascular morbidity and mortality,[19] increases in PAP pressure to decrease the AHI to < 5 events/hour may not be indicated if adherence to therapy is reduced concomitantly. Additional studies will be needed to address this issue.

Despite these findings, attended manual titration polysomnograms remain the gold standard for determining CPAP treatment pressures,[20] even though titration pressures are known to have several limitations.[21] Typically, acceptable titration studies generate the highest pressure required to eliminate all obstructive respiratory events, including snoring. This pressure is not necessarily needed throughout a single night or on a night to night basis due to several factors, including sleep position, sleep stage, alcohol use, medications, and exercise.[11,21] Our findings suggest that, in most cases, split-night or full-night polysomnograms are not necessary to initiate PAP therapy for patients with uncomplicated OSA.

We found that patients with a higher BMI were more likely to have higher P_{TIT} when compared with $P_{90\text{-}95}$. BMI has been shown to be independently associated with CPAP titration level.[11,13,22] BMI > 35 kg/m^2 has been identified as a predictor of lower rates of successful CPAP titration.[23] As such, BMI has been incorporated into several equations designed to predict optimal CPAP settings.[22,24] Given our findings, a trial of APAP may be an alternative in obese patients with uncomplicated OSA in whom a therapeutic P_{TIT} cannot be determined during a manual CPAP titration, as pressure requirements may be overestimated.

In our study population, the residual AHI on APAP was lower than the residual AHI observed at P_{TIT} during manual CPAP titration studies. Notably, this finding was observed despite APAP titration algorithms that automatically lower PAP in the absence of hypopneas and apneas, thus permitting them to transiently recur. This observation is consistent with prior studies that have shown that automatic titration is at least as effective as standard manual titration in improving AHI.[8,9,15,25]

We acknowledge that a major limitation of our study was that it was retrospective and nonrandomized. In addition, data from the devices of 2 manufacturers of APAP devices were combined; APAP algorithms and the reported surrogate PAPs, $P_{90\text{-}95}$, are different. However, we did not observe any systematic differences in our observations between the devices. In addition, we did not assess any potential impact of mask leak on pressures. Large leaks may adversely impact PAP adherence and may have affected pressure requirements. Despite the aforementioned limitations, our study provides a large systematic comparison of therapeutic pressures determined during a manual CPAP titration and those obtained during a trial of APAP.

In conclusion, split- and full-night titrations may overestimate pressure requirements, particularly in patients with higher BMIs, and may not be necessary in managing patients with uncomplicated OSA. APAP appears to be at least as effective as single-pressure CPAP, while delivering lower PAP.

ABBREVIATIONS

APAP, auto-titrating positive airway pressure
BMI, body mass index
CPAP, continuous positive airway pressure
OSA, obstructive sleep apnea
PAP, positive airway pressure
P_{TIT}, manually derived CPAP therapeutic pressure
$P_{90\text{-}95}$, automatically derived 90th or 95th percentile pressure

REFERENCES

1. 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.
2. Kushida CA, Littner MR, Hirshkowitz M, et al; American Academy of Sleep Medicine. Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. *Sleep.* 2006;29 (3):375–380.
3. Littner M, Hirshkowitz M, Davila D, et al; Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the use of auto-titrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome. An American Academy of Sleep Medicine report. *Sleep.* 2002;25(2):143–147.
4. 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.
5. Wolkove N, Baltzan M, Kamel H, Dabrusin R, Palayew M. Long-term compliance with continuous positive airway pressure in patients with obstructive sleep apnea. *Can Respir J.* 2008;15(7):365–369.
6. Gulati A, Oscroft N, Chadwick R, Ali M, Smith I. The impact of changing people with sleep apnea using CPAP less than 4 h per night to a bi-level device. *Respir Med.* 2015; 109(6):778–783.
7. Nigam G, Pathak C, Riaz M. A systematic review on prevalence and risk factors associated with treatment- emergent central sleep apnea. *Ann Thorac Med.* 2016;11 (3):202–210.
8. Pływaczewski R, Zgierska A, Bednarek M, Zieliński J. Comparison of automatic (AUTO-CPAP) and "manual" CPAP pressure titration in patients with obstructive sleep apnea. Article in Polish. *Pneumonol Alergol Pol.* 2000;68(5-6):232–237.
9. Randerath W, Parys K, Lehmann D, Sanner B, Feldmeyer F, Rühle K-H. Self-adjusting continuous positive airway pressure therapy based on the measurement of impedance: a comparison of free pressure variation and individually fixed higher minimum pressure. *Respiration.* 2000;67(3):272–279.
10. Teschler H, Wessendorf T, Farhat A, Konietzko N, Berthon-Jones M. Two months auto-adjusting vs conventional nCPAP for obstructive sleep apnoea syndrome. *Eur Respir J.* 2000;15(6):990–995.
11. Kim H, Lee M, Hwangbo Y, Yang KI. Automatic derivation of continuous positive airway pressure settings: comparison with in-laboratory titration. *J Clin Neurol.* 2020; 16(2):314–320.
12. Wongsritrang K, Fueangkamloon S. Comparison of the clinical outcomes between unattended home APAP and polysomnography manual titration in obstructive sleep apnea patients. *J Med Assoc Thai.* 2013;96(9):1159–1163.
13. Xie H-S, Chen G-P, Huang JF, et al. Impact of upper airway configuration on CPAP titration assessed by CT during Müller's maneuver in OSA patients. *Respir Physiol Neurobiol.* 2021;284:103559.
14. Ghrairi H, Khalfallah I, Abid N, Loukil M. Adherence to treatment with continuous positive airways pressure. Article in French. *Rev Mal Respir.* 2018;35(5):531–537.
15. Gao W, Jin Y, Wang Y, et al. Is automatic CPAP titration as effective as manual CPAP titration in OSAHS patients? A meta-analysis. *Sleep Breath.* 2012;16(2):329–340.
16. Kim JH, Kwon MS, Song HM, Lee B-J, Jang YJ, Chung Y-S. Compliance with positive airway pressure treatment for obstructive sleep apnea. *Clin Exp Otorhinolaryngol.* 2009;2(2):90–96.

17. Mulgrew AT, Lawati NA, Ayas NT, et al. Residual sleep apnea on polysomnography after 3 months of CPAP therapy: clinical implications, predictors and patterns. *Sleep Med.* 2010;11(2):119–125.
18. Bailly S, Daabek N, Jullian-Desayes I, et al. Partial failure of CPAP treatment for sleep apnoea: analysis of the French national sleep database. *Respirology.* 2020;25(1): 104–111.
19. Chowdhuri S, Quan SF, Almeida F, et al; ATS Ad Hoc Committee on Mild Obstructive Sleep Apnea. An official American Thoracic Society research statement: impact of mild obstructive sleep apnea in adults. *Am J Respir Crit Care Med.* 2016;193(9): e37–e54.
20. Lopez-Campos JL, Garcia Polo C, Leon Jimenez A, Gonzalez-Moya E, Arnedillo A, Fernandez Berni JJ. CPAP titration: different methods for similar clinical results. *Eur J Intern Med.* 2007;18(3):230–234.
21. Khaytin I, Tapia IE, Xanthopoulos MS, et al. Auto-titrating CPAP for the treatment of obstructive sleep apnea in children. *J Clin Sleep Med.* 2020; 16(6):871–878.
22. 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.
23. BaHammam AS, ALAnbay E, Alrajhi N, Olaish AH. The success rate of split-night polysomnography and its impact on continuous positive airway pressure compliance. *Ann Thorac Med.* 2015;10(4):274–278.
24. 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.
25. Resta O, Carratù P, Depalo A, et al. Effects of fixed compared to automatic CPAP on sleep in obstructive sleep apnoea syndrome. *Monaldi Arch Chest Dis.* 2004;61(3): 153–156.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication February 2, 2021
Submitted in final revised form March 26, 2021
Accepted for publication March 26, 2021
Address correspondence to: Olabimpe S. Fashanu, MD, MPH, Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, Harvard Medical School, 231 Longwood Avenue, Boston, MA 02115; Email: ofashanu@bwh.harvard.edu

DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. Work for this study was performed at the Brigham and Women's Hospital in Boston, Massachusetts. Stuart F. Quan is a consultant for Jazz Pharmaceuticals, Best Doctors, and Whispersom. All other authors report no conflicts of interest.