JCN Open Access ORIGINAL ARTICLE

pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2020;16(1):90-95 / https://doi.org/10.3988/jcn.2020.16.1.90

Effective Continuous Positive Airway Pressure Changes Related to Sleep Stage and Body Position in Obstructive Sleep Apnea during Upward and Downward Titration: An Experimental Study

Eun-Mi Lee[a*]
Tae-Hoon Lee[b*]
Ol-Lim Park[a]
Jung Gwon Nam[b]

[a]Departments of Neurology and [b]Otorhinolaryngology-Head and Neck Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea

Background and Purpose The aim of this study was to determine how the sleep stage and body position influence the effective pressure (Peff) in standard upward titration and experimental downward titration.

Methods This study applied successful manual titration of continuous positive airway pressure over 3 hours [including at least 15 min in supine rapid eye movement (REM) sleep] followed by consecutive downward titration for at least 1 hour to 22 patients with moderate-to-severe obstructive sleep apnea. We analyzed baseline polysomnography variables and compared the effective pressures ($Peff1_{upward}$ and $Peff2_{downward}$) between non-REM and REM sleep and between supine and lateral positions using the paired *t*-test or Wilcoxon signed-rank test.

Results During upward titration, Peff1 increased during REM sleep compared to non-REM sleep [9.5±2.9 vs. 8.9±2.7 cm H_2O (mean±SD), $\Delta Peff1_{REM-non\text{-}REM}$=0.6±1.1 cm H_2O; p=0.024]. During downward titration, Peff2 was higher in a supine than a lateral position (7.3±1.7 vs. 4.8±1.5 cm H_2O, $\Delta Peff2_{supine\text{-}lateral}$=2.5±1.3 cm H_2O; p=0.068). When comparing both upward and downward titration conditions, we found that Peff2 was significantly lower than Peff1 in all sleep stages, especially during REM sleep ($Peff1_{REM}$ vs. $Peff2_{REM}$=9.5±2.9 vs. 7.4±3.3 cm H_2O) with an overall difference of 2.1±1.7 cm H_2O (p<0.001). Peff in supine sleep decreased from 9.4±3.0 cm H_2O ($Peff1_{supine}$) to 7.6±3.3 cm H_2O ($Peff2_{supine}$), with an overall difference of 1.8±1.6 cm H_2O (p<0.001).

Conclusions This study has revealed that the collapsibility of the upper airway is influenced by sleep stage and body position. After achieving an initial Peff1, a lower pressure was acceptable to maintain airway patency during the rest of the sleep. The observed pressure decrease may support the use of an automated titration device that integrates real-time positional and sleep-stage factors, and the use of a lower pressure may improve fixed-pressure-related intolerance.

Key Words obstructive sleep apnea, continuous positive airway pressure, sleep position, sleep stages.

Received June 12, 2019
Revised September 18, 2019
Accepted September 20, 2019

Correspondence
Jung Gwon Nam, MD, PhD
Department of Otorhinolaryngology-Head and Neck Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, 877 Bangeojinsunhwando-ro, Dong-gu, Ulsan 44033, Korea
Tel +82-52-250-7180
Fax +82-52-234-7182
E-mail jknam0266@naver.com

*These authors contributed equally to this work.

INTRODUCTION

Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnea (OSA). The pressure required to normalize breathing during sleep is called the effective pressure (Peff), and this is influenced by several factors such as the anatomy and collapsibility upper airway of the individual subject, hysteresis of the upper airway, changes in body position, sleep stage, and weight changes. Among these factors, it is well known that

higher pressures are required during rapid eye movement (REM) sleep and when sleeping in a supine position,[1] and so CPAP titration guidelines recommend a certain Peff level to maintain the airway patency focused on the most vulnerable supine REM sleep. However, the positive pressure required may change throughout the night due to changes in body position and sleep stage.

There is evidence that the optimal CPAP level in a supine position is more than 2 cm H_2O higher than that needed while sleeping in a lateral position, while it does not differ with sleep stage, obesity, or age.[1] Indeed, a CPAP higher than necessary for the rest of the night might negatively affect CPAP adherence, and so it is important to determine the minimum Peff depending on sleep stage and body position. Moreover, the upper airway exhibits hysteresis, which accounts for a decrease in the effective positive pressure level once an initial Peff setting has been reached.[2] Thus, supine REM sleep targeting a single pressure is usually higher that necessary for the rest of the night, and hence is overpressured in the strict sense.

Data are scarce on how the Peff varies with body position and sleep stage in CPAP manual upward and downward titration. The aim of this study was to determine the effects of sleep stage and body position on the Peff level during CPAP standard upward and experimental downward titration in 22 patients with moderate-to-severe OSA.

METHODS

Patient selection and study design

The study had a prospective experimental design. The included patients were adults diagnosed with uncomplicated moderate-to-severe OSA who had signs and symptoms of OSA and who visited the sleep laboratory in order to undergo CPAP titration at Ulsan University Hospital between September 2017 and June 2018. The following inclusion criteria were applied: 1) older than 19 years with moderate-to-severe sleep apnea-hypopnea, defined as an apnea-hypopnea index (AHI) of ≥15 in baseline diagnostic overnight polysomnography (PSG), 2) total sleep time of >3 hours during CPAP upward titration with successful (optimal-to-good grade) manual titration, and 3) total sleep time of >1 hour during CPAP downward titration including supine REM sleep for >15 min. The exclusion criterion was not achieving satisfactory titration during the initial 3 hours of sleep.

Forty patients agreed with participate to this study and signed an informed consent form. Twelve patients withdrew their consent prior to undergoing CPAP (reasons not provided). A further six patients were excluded due to not achieving satisfactory titration during CPAP upward titration and a short total sleep time of <1 hour during CPAP downward titration. Therefore, 22 patients who were consistent with the inclusion criteria finally completed CPAP downward titration. The study protocol was approved by the Institutional Review Board of Ulsan Univeristy Hospital (IRB No. UUH 2017-08-009).

Diagnostic overnight PSG

OSA diagnoses were made using standard PSG (Comet-Plus, Astro-Med, Inc.,West Warwick, RI, USA), which included electroencephalography, electrooculography, electromyography, electrocardiography, pulse oxymetry for oxygen saturation, and a microphone to detect snoring. The airflow was measured using an oronasal thermistor and a nasal pressure transducer, and the respiratory effort of thoracoabdominal movement was measured using respiratory inductance plethysmography. Sleep and associated events were scored according to the American Academy of Sleep Medicine manual.[3] The AHI was defined as the average number of episodes of apnea and hypopnea per hour of total sleep time. Apnea was defined as a decrease in the peak thermal sensor excursion by at least 90% from baseline for at least 10 seconds. A hypopnea episode was defined as a decrease in the nasal pressure signal by at least 30% from baseline for at least 10 seconds, with a reduction in O_2 saturation of at least 4% from the pre-event baseline. Age, sex, body mass index, and neck circumference were recorded at the time of the baseline diagnostic overnight PSG.

CPAP upward titration

CPAP titration studies were performed by a sleep technologist in laboratory PSG (S9 CPAP device, ResMed, San Diego, SA, USA). CPAP was manually titrated to the lowest effective CPAP level based on clinical guidelines.[4] The starting CPAP was 4 cm H_2O, and upward titration in ≥1-cm-H_2O increments over ≥5-min periods continued according to the breathing events observed until a period of ≥30 min without breathing events was achieved. CPAP was increased if there were two obstructive apnea episodes, three hypopnea episodes, or five respiratory-effort-related arousals, or at least 3 min of loud or unambiguous snoring.[4] If the patient woke up and complained that the pressure was too high, it was restarted at a lower pressure that was comfortable enough to allow the patient to return to sleep. The titrated CPAP level was defined as the lowest effective pressure (Peff1). Optimal titration and good titration were respectively defined as a respiratory disturbance index (RDI) of <5/hour for at least 15 min including supine REM sleep and an RDI of ≤10/hour or by 50% if the baseline RDI was

<15/hour including supine REM sleep at the selected pressure without continuous interruption by spontaneous arousals or awakenings. The duration of each sleep period (N1, N2, N3, and REM), total sleep time, the duration in a supine and lateral position, Peff1 during REM and non-REM sleep, Peff1 in a supine and lateral position, and AHI at Peff1 during CPAP upward titration were measured.

CPAP downward titration

CPAP downward titration was applied to patients who underwent successful optimal or good CPAP titration (including at least 15 min in supine REM sleep at the selected pressure) for longer than 3 hours. After ≥30 min had elapsed without breathing events at the selected pressure, CPAP was decreased by 1 cm H_2O over an interval ≥10 min until there was re-emergence of obstructive respiratory events. Upward titration was then continued in ≥1-cm H_2O increments over ≥5 min. The second pressure level that resulted in the abolition of abnormal respiratory events and snoring based on clinical guidelines was defined as Peff2. Downward titration was performed for at least 1 hour and included ≥15 min of supine REM sleep. The duration of each sleep period (N1, N2, N3, and REM), total sleep time, the duration in a supine and lateral position, Peff2 during REM and non-REM sleep, Peff2 in a supine and lateral position, and AHI at Peff2 during CPAP downward titration were measured.

Statistical analysis

All data are presented as mean±SD values for continuous variables. The presence of variance normality was verified to ensure that the correct statistical tests were applied. The paired *t*-test or Wilcoxon signed-rank test was used to compare between CPAP upward vs. downward measurements, supine vs. lateral body positions, and non-REM vs. REM sleep in each CPAP upward–downward titration. Statistical analysis was performed using SPSS (version 25.0, IBM Corp., Armonk, NY, USA), and $p<0.05$ was considered statistically significant.

RESULTS

Characteristics of patients

This study enrolled 22 patients (20 males and 2 females) aged 50.6±11.1 years and with an AHI in diagnostic PSG of 45.9±24.2/hour. The anthropometric and PSG measurements of participating patients are summarized in Table 1 and Table 2.

CPAP upward titration

The total duration of CPAP upward titration was 220.6±48.2 min, which included 47.6±19.2 min (range, 15–84.5 min) of REM sleep. Eighteen of the 22 patients slept only in a supine position during the upward titration, with the other 4 patients sleeping in both supine and lateral positions. Peff1 (i.e., Peff during REM sleep) was 9.5±2.9 cm H_2O, at which AHI was 2.0±3.2 cm H_2O. The required pressure peaked during REM and when sleeping in a supine position in all but one of the patients. Peff1 was significantly higher during REM than non-REM sleep, with an overall difference of 0.6±1.1 cm H_2O ($p=0.024$). Peff1 change from the supine to lateral position showed no statistically significant differences ($p=0.109$).

CPAP downward titration

The positive pressure level could be decreased in all 22 patients after Peff1 had been determined. The total duration of CPAP downward titration was 94.7±20.6 min, which included 29.5±10.9 min (range, 15–56 min) of REM sleep. Eighteen of the 22 patients slept only in a supine position during downward titration, with the other 4 patients sleeping in both supine and lateral positions. Peff2 (i.e., Peff during REM sleep) was 7.4±3.3 cm H_2O, and downward titration had no harmful effect on the AHI (AHI in Peff2, 1.4±2.4 cm H_2O) or on oxygen saturation. Peff2 did not differ between REM

Table 1. Anthropometric and overnight PSG characteristics of the study population (*n*=22)

Characteristic	Value
Age, years	50.6±11.1
Sex, male:female	20:2
Neck circumference, cm	40.4±4.6
Body mass index, kg/m^2	27.0±4.8
Positional dependency	9/12
REM dependency	3/22

PSG variable	Overnight PSG	Upward titration	Downward titration
TST, min	297.3±70.8	220.6±48.2	94.7±20.6
Sleep-stage duration, min			
N1	100.2±55.3	31.1±14.2	7.1±4.3
N2	138.7±55.0	110.0±37.2	51.4±19.6
N3	26.3±36.3	36.4±25.5	6.7±9.9
Non-REM (N1+N2+N3)	243.7±54.7	173.0±45.2	65.2±21.8
REM	53.6±33.8	47.6±19.2	29.5±10.9
Duration of sleep position, min			
Lateral	78.4±89.0	20.7±48.2	6.3±15.3
Supine	224.0±92.8	209.2±52.5	88.4±24.9
AHI at baseline or Peff	45.9±24.2	2.0±3.2	1.4±2.4

Data are *n* or mean±SD values.
AHI: apnea-hypopnea index (apnea and hypopnea episodes per hour of sleep), Peff: effective pressure, PSG: polysomnography, REM: rapid eye movement, TST: total sleep time.

Table 2. Changes in Peff with sleep stage and body position during CPAP upward and downward titration

Sleep variable	*n*	Peff, cm H_2O	ΔPeff	*p*	AHI in Peff	*p*
CPAP upward titration						
REM	22	9.5±2.9	0.6±1.1	0.024	2.0±3.2	n.s.
Non-REM	22	8.9±2.7			1.2±2.0	
Supine	4	9.4±3.0	2.0±2.2	0.109	2.2±3.9	n.s.
Lateral	4	7.0±3.6			2.7±4.1	
CPAP downward titration						
REM	22	7.4±3.3	0.0±1.7	0.903	1.4±2.4	n.s.
Non-REM	22	7.4±3.0			2.0±2.6	
Supine	4	7.3±1.7	2.5±1.3	0.068	2.7±3.8	n.s.
Lateral	4	4.8±1.5			2.0±3.2	

Data are mean±SD values.
AHI: apnea-hypopnea index, CPAP: continuous positive airway pressure, n.s.: not significant, Peff: effective pressure, REM: rapid eye movement.

Table 3. Comparison of Peff during CPAP upward and downward titration

Sleep variable	Non-REM (*n*=22)	REM (*n*=22)	Lateral position (*n*=2)	Supine position (*n*=22)
Peff1	8.9±2.7	9.5±2.9	7.0±3.6	9.4±3.0
Peff2	7.4±3.0	7.4±3.3	4.8±1.5	7.6±3.3
Δ(Peff1–Peff2)	1.5±1.6	2.1±1.7	−1.0±1.4	1.8±1.6
p	<0.001	<0.001	n.a.	<0.001

Data are mean±SD values.
CPAP: continuous positive airway pressure, n.a., not applicable, REM: rapid eye movement.

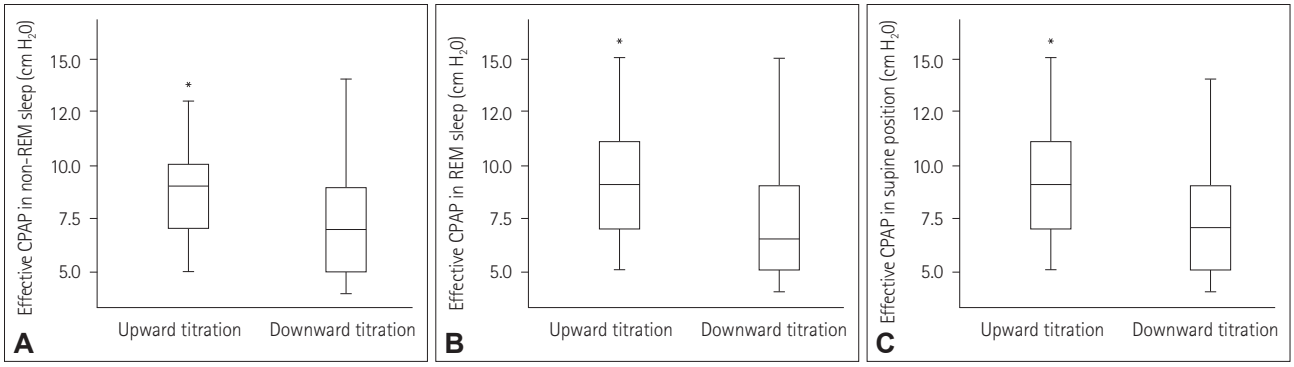

Fig. 1. Comparison of Peff during CPAP upward and downward titration (A: Non-REM, B: REM, C: Supine position). Data are mean and standard-error values. **p*<0.05 (A-C). CPAP: continuous positive airway pressure, Peff: effective pressure, REM: rapid eye movement.

and non-REM sleep (7.4±3.3 vs. 7.4±3.0 cm H_2O, p=0.903). Peff change between supine and lateral position showed marginally significant power, with an overall difference of 2.5±1.3 cmH_2O (p=0.068).

CPAP upward vs. downward titration

Peff2 during experimental CPAP downward titration was significantly lower than Peff1 during standard CPAP upward titration in all sleep stages ($Peff1_{Non\text{-}REM}$ vs. $Peff2_{Non\text{-}REM}$, 8.9±2.7 vs. 7.4±3.0 cm H_2O; $Peff1_{REM}$ vs. $Peff2_{REM}$, 9.5±2.9 vs. 7.4±3.3 cm H_2O) (Table 3, Fig.1). The difference Peff1–Peff2 was higher during REM sleep (2.1±1.7 cm H_2O, p<0.001) than during non-REM sleep (1.5±1.6 cm H_2O, p<0.001). Peff2 in a supine position was also significantly lower than Peff1 in a supine position, with an overall difference of 1.8±1.6 cm H_2O (p<0.001). The difference in Peff in a lateral position could not be analyzed due to the small number of samples (n=2).

DISCUSSION

This study investigated how the sleep stage and body position influenced CPAP standard upward and experimental downward titration in 22 patients with moderate-to-severe OSA. The novel methodology aspect of this study is that it is the first to compare the effects of changes in sleep stage

and body position on upward titration followed by consecutive downward titration.

Several clinically relevant findings were obtained. First, the sleep stage influenced the optimal pressure, with a predisposition toward a higher pressure during REM sleep compared to non-REM sleep during standard upward titration, although in contrast to our expectations this effect was modest ($\Delta Peff1_{REM\text{-}non\text{-}REM}$=0.6±1.1 cm H_2O). Second, the effect of body position on decreasing the pressure was only weakly or marginally significant, but this could have been due to the small number of analyzable patients. Third, the Peff level can be significantly decreased by more than 1.5 cm H_2O using downward titration in all sleep stages, and especially during REM sleep in a supine position without AHI aggravation.

It is generally accepted that higher pressures are required to reverse airway collapse during REM sleep and when the patient sleeps in a supine position,[1] and so a fixed CPAP aims to eliminate abnormal respiratory events during the most vulnerable supine REM period. Our results are consistent previous studies finding that Peff1 was highest during REM sleep during upward titration and that Peff2 was similar in REM and non-REM sleep during downward titration.

A supine sleep position is consistently found to be an aggravating factor for OSA. Positional sleep apnea has reportedly been found in 7−50% of patients with OSA, with it being significantly more common when sleep apnea was mild than when it was moderate or severe.[5] All of our 22 patients had moderate-to-severe OSA, with a mean AHI of >45/hour. Considering high burden of OSA, the baseline PSG findings showed non-position-dependent OSA in almost half of patients and remained 9 of the 12 patients exhibished positional OSA. Some studies have demonstrated OSA improvement in a lateral or nonsupine position, with the closing pressure decreasing by an average of 2−3 cm H_2O in a lateral position.[6,7] Therefore, the optimal required CPAP can be significantly lower for positional than for nonpositional patients. A previous study[8] found that the mean effective nasal CPAP level was lower in the positional than in the nonpositional group (8.0 vs. 9.1 cm H_2O, p<0.05). Our study found that Peff in a supine position was higher than that in a lateral position, with an overall differences of 2.0±2.2 and 2.5±1.3 cm H_2O for upward and downward titration, respectively, but this effect was only weakly or marginally significant. Only 4 of the 22 (18.2%) patients slept in both postures during each titration condition, and so the number of patients exhibiting positional changes during upward and downward titration was too small for sensitively detecting significant differences in our study. However, it is expected that among a large number of patients with positional dependency, a lateral sleep position would require the lowest pressure.

A particularly important result of this study was the significant reduction in pressure during downward titration. Peff2 during REM sleep was significantly lower than Peff1 during REM sleep, with an overall difference of 2.1±1.7 cm H_2O, and Peff2 during supine sleep was also significantly lower than Peff1 during supine sleep, with an overall difference of 1.8±1.6 cm H_2O. The hysteresis phenomenon could be responsible for this difference[2]: during CPAP upward titration at which flow limitation disappears is 2−5 cm H_2O higher than the level at which it reappears during downward titration. This hysteresis effect associated with the discrepancy in airway opening and closing pressures means that a lower pressure or energy is required to maintain the patency of the upper airway during downward titration. One study involving 85 OSA patients used CPAP downward titration until respiratory abnormalities re-emerged after reaching the Peff1, and found that Peff2 was significantly lower than Peff1, with an overall difference of 0.6±1.5 cm H_2O.[9] In the present study there was a prominent CPAP downward titration effect, with a mean difference of approximately 2 cm H_2O. This situation leads to the lowest Peff that maintains upper airway patency being used during the late period of sleep. The residual AHI during downward titration was similar to that during upward titration, at <5/hour, and so the efficacy of CPAP downward titration was not inferior to that of standard upward titration. Using a fixed higher pressure throughout the night might be expected to increase mask leaks, pressure intolerance, and possibly also reduce the acceptance and utilization of PAP. For this reason, an autoadjustable device was developed to provide the minimum Peff throughout the sleep period, and the efficacy of auto-PAP was comparable to that of CPAP in mild-to-moderate OSA.[10]

This study was subject to some limitations. First, the number of enrolled patients was too small to provide a high statistical power. The high withdrawal rate of informed consents and the application of strict sleep-time criteria to satisfy both upward and downward titration in single-split nighttime PSG were the main reasons for the smallness of the sample in our study. Second, the effects of body position could not be characterized in 18 patients whose body positions did not change during titration. These subjects were excluded from the Peff comparisons of positional effects in upward and downward titration. Furthermore, the time spent in a lateral position was disproportionately short compared to that in a supine position during both upward and downward titration, and so we cannot draw strong conclusions about positional effects during titration. To permit a stable body position during an extended sleep time, two separated full-night PSG sessions

composed of each upward and downward titration are required to clarify the effect of changes in sleep stage and body position, and to reconfirm the pressure-reducing effect during downward titration in future investigations. Fourth, even though this study demonstrated a pressure-lowering effect of 1.5−2 cm H_2O during downward titration, we were unable to determine whether the reduced PAP really influenced patient adherence.

Commercially available autotitrating PAP devices utilize various algorithms to determine when and by how much to increase or decrease the pressure according to the respiratory dynamics. The development of PAP devices that include algorithms that sense body position or the appearance of REM sleep could reveal the optimal preset decrement or increment pressure level for providing more detailed and personalized PAP. The pressure decrease observed in our study may support an autotitration device that integrates real-time positional and sleep-stage factors and the use of the lowest pressure to improve fixed-pressure-related intolerance.

Author Contributions

Conceptualization: Eun-Mi Lee, Tae-Hoon Lee, Jung Gwon Nam. Formal analysis: Eun-Mi Lee. Funding acquisition: Tae-Hoon Lee, Jung Gwon Nam. Investigation: Eun-Mi Lee, Ol-Lim Park. Methodology: Eun-Mi Lee, Tae-Hoon Lee, Jung Gwon Nam. Resources: Tae-Hoon Lee, Jung Gwon Nam. Supervision: Eun-Mi Lee, Tae-Hoon Lee, Jung Gwon Nam. Writing—original draft: Eun-Mi Lee, Tae-Hoon Lee. Writing—review & editing: Eun-Mi Lee, Tae-Hoon Lee, Jung Gwon Nam.

ORCID iDs

Eun-Mi Lee	https://orcid.org/0000-0001-6423-0081
Tae-Hoon Lee	https://orcid.org/0000-0003-1395-5677
Ol-Lim Park	https://orcid.org/0000-0002-2455-4142
Jung Gwon Nam	https://orcid.org/0000-0002-6556-9084

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Acknowledgements

This study was supported by a grant from the Korean Ministry of Trade, Industry and Energy (grant number: 10077827).

REFERENCES

1. Oksenberg A, Silverberg DS, Arons E, Radwan H. The sleep supine position has a major effect on optimal nasal continuous positive airway pressure : relationship with rapid eye movements and non-rapid eye movements sleep, body mass index, respiratory disturbance index, and age. *Chest* 1999;116:1000-1006.
2. Condos R, Norman RG, Krishnasamy I, Peduzzi N, Goldring RM, Rapoport DM. Flow limitation as a noninvasive assessment of residual upper-airway resistance during continuous positive airway pressure therapy of obstructive sleep apnea. *Am J Respir Crit Care Med* 1994;150:475-480.
3. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2012;8:597-619.
4. Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. *J Clin Sleep Med* 2008;4:157-171.
5. Mador MJ, Kufel TJ, Magalang UJ, Rajesh SK, Watwe V, Grant BJ. Prevalence of positional sleep apnea in patients undergoing polysomnography. *Chest* 2005;128:2130-2137.
6. Isono S, Tanaka A, Nishino T. Lateral position decreases collapsibility of the passive pharynx in patients with obstructive sleep apnea. *Anesthesiology* 2002;97:780-785.
7. Penzel T, Möller M, Becker HF, Knaack L, Peter JH. Effect of sleep position and sleep stage on the collapsibility of the upper airways in patients with sleep apnea. *Sleep* 2001;24:90-95.
8. Pevernagie DA, Shepard JW Jr. Relations between sleep stage, posture and effective nasal CPAP levels in OSA. *Sleep* 1992;15:162-167.
9. Bureau MP, Sériès F. Comparison of two in-laboratory titration methods to determine effective pressure levels in patients with obstructive sleep apnoea. *Thorax* 2000;55:741-745.
10. Nolan GM, Doherty LS, Mc Nicholas WT. Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. *Sleep* 2007;30:189-194.