

Restarting CPAP Therapy for Sleep Apnea After a Previous Failure

Heidi Avellan-Hietanen, Paula Maasilta, and Adel Bachour

BACKGROUND: About one third of patients fail their first CPAP trial due to several factors. Despite its clinical importance, data on the success of CPAP re-initiation are scarce. **METHODS:** Of the 6,231 patients referred to our sleep unit for sleep apnea, we included 224 subjects referred for re-initiation of CPAP therapy (re-CPAP). The control group consisted of 228 CPAP-naïve subjects referred for CPAP initiation. Data on subject characteristics, sleep study, and CPAP outcome were collected. **RESULTS:** The re-CPAP group had more severe apnea than the control group. After at least 1 y of CPAP therapy, 52% of the re-CPAP group stayed on therapy; this was significantly lower than the 67% adherence for the control group ($P = .001$). No gender difference was observed in the control group ($P = .12$), whereas women in the re-CPAP group remained on therapy significantly less than men ($P = .002$). **CONCLUSIONS:** The percentage of subjects who stayed on CPAP therapy after 1 y was significantly reduced when CPAP was re-initiated compared to the control group. CPAP acceptance after re-initiation was higher among men than women. Further studies are necessary to explain this gender difference. *Key words:* CPAP; gender; outpatient; sleep apnea; CPAP initiation; re-initiation; adherence. [Respir Care 2020;65(10):1541–1546. © 2020 Daedalus Enterprises]

Introduction

CPAP is the accepted standard treatment for obstructive sleep apnea. Adherence to CPAP therapy is generally poor. Only 70% of CPAP-naïve patients continue to use CPAP regularly after 1 year.¹ When CPAP therapy fails, both the doctor and the patient discuss the next alternative therapy choice. Surgery is not currently routine but may be useful in special conditions, such as tonsillar hypertrophy.² An oral appliance is a good alternative therapeutic option and has relatively acceptable adherence and efficacy, particularly in patients with less severe obstructive sleep apnea and normal body mass index.³ Recently, upper airway stimulator therapy has emerged as an alternative therapy for those who fail CPAP.⁴ However, upper airway stimulator is currently restricted to select patients and is not applicable for those with body mass index $> 35 \text{ kg/m}^2$.

The reasons for CPAP failure are multifactorial and include claustrophobia, poor mask fit, nasal obstruction, insomnia, and lack of motivation.⁵ These factors may evolve over time, which suggests that a new CPAP trial after a first failure may be successful.

Because CPAP is safe and noninvasive, re-initiation after previous failure is always an alternative. We hypothesized that CPAP adherence is lower in individuals who have tried CPAP before than in CPAP-naïve patients. The cost of CPAP initiation is considerable, so it is important to evaluate the success rate of CPAP therapy re-initiation and its cost.⁶

Failure of alternative therapies is a reason to attempt CPAP again. Moreover, symptoms may subside after surgery but relapse a few years later, especially after weight gain. Although a CPAP re-initiation trial is often proposed when symptoms relapse, the success rate of such a trial is unknown. Although current technology offers better CPAP devices and more suitable facial interfaces that may improve CPAP adherence, the roles of such technologies in improving CPAP adherence was previously reported to be modest.⁷

Methods

Our sleep unit is based in the Heart and Lung Center (a tertiary teaching university hospital) in Helsinki, Finland. Physicians at the pulmonary department also rotate in the sleep unit. The rotating physicians in the sleep unit did not

The authors are affiliated with the Sleep Unit, Heart and Lung Centre, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.

This work was partially supported by the Helsinki University Hospital Research Fund. The authors have disclosed no conflicts of interest.

Correspondence: Heidi Avellan-Hietanen MD. E-mail: heidi.avellan-hietanen@hus.fi.

DOI: 10.4187/respcare.07766

participate in the recruitment of subjects. The recruitment was performed over 5 y and ended in 2016. Ethical committee approval number 592/2005, DNRO 389/E5/05, research committee approval M101060014, DNRO 81/2008.

During the 5-y recruitment study, a total of 6,231 patients were referred to our sleep unit for suspicion of sleep apnea or treatment of sleep apnea. In a previous study, we reported that 62.8% of our referred patients initiated CPAP.⁸ Therefore, the total number of CPAP initiations in our sleep unit during the 5-y study was 3,913. A total of 224 subjects attempted CPAP re-initiation within a period of ≥ 6 months following CPAP failure. CPAP re-initiation was estimated to be about 11% of the total CPAP initiations in our clinic. Data on age, apnea index, sleep study, Epworth sleepiness scale (ESS), comorbidities, and CPAP adherence were recorded to evaluate CPAP adherence in the CPAP re-initiation (re-CPAP) group.

For the control group, we randomly selected 228 subjects from patients referred to our clinic who underwent CPAP initiation for the first time in 2015. All subjects in the control group were CPAP-naïve patients who underwent CPAP re-initiation within a period of 6 months after a previous failure were excluded (Fig. 1).

We considered CPAP therapy as failed when the patient discontinued the therapy and returned the CPAP device to the hospital regardless of the time spent between initiation and discontinuation. In the United States, the patient must fulfill specific Medicaid requirements for continuation of CPAP therapy after the initial period. If the patient fails to fulfill these requirements, CPAP therapy is considered failed. Medicaid reimbursement requires re-evaluation after first failure. The time lapse between CPAP failure and re-initiation is evaluated to be at least 6 months.

CPAP Initiation

The indication for initiating CPAP therapy to treat obstructive sleep apnea was a respiratory event index of ≥ 15 events/h or ≥ 5 events/h if the subject had daytime hypersomnolence or significant comorbidities. Subjects starting CPAP underwent a 1-h familiarization session at the sleep clinic with the CPAP device and masks as described previously.⁹ Subjects were assessed at 2–3 months after CPAP initiation to ensure good therapy response. Thereafter, follow-up contacts were routinely planned annually.¹⁰ We used ResMed autoCPAP devices (Resmed, San Diego, California). In 2014, humidification was integrated into the Resmed CPAP device. Therefore, we recommend CPAP with humidification to all our patients. Before that time, humidification was offered to patients suffering from any degree of nasal obstruction.

QUICK LOOK

Current knowledge

CPAP therapy fails within 1 year of initiation in about one third of patients. There is minimal data about the success of CPAP when re-initiated. Intolerance secondary to discomfort is a leading cause of failure.

What this paper contributes to our knowledge

The percentage of subjects who stayed on CPAP after re-initiation was 60% in men and 38% in women. Gender significantly influenced the success of CPAP re-initiation. Additional follow-up in women is warranted.

CPAP Regulations in Finland

In Finland, CPAP devices and interfaces are purchased by the hospital following competitive tendering as stipulated in public procurement legislation. The public hospitals thus own the CPAP devices, which are then offered to patients free of charge. If the patient forgoes treatment, he or she must return the device to the clinic.¹⁰ Once CPAP therapy is initiated, there is no requirement by the national insurance for a regular prescription renewal by the physician. The national CPAP instructions recommend a regular follow-up with a physician or nurse.¹¹ In Finland there is no requirement for the physician to renew the CPAP prescription. There is no cut-off point regarding daily CPAP that is used to decide the continuation of CPAP therapy because the medical team always hopes that the patient will have sufficient motivation for future regular use of the device. The patient may therefore keep the device as long as he or she is willing to utilize the therapy.

Statistical Analysis

Analysis of variance, chi-square test, and *t* test were used when appropriate. $P < .05$ was considered statistically significant. We used SPSS (Version 25; IBM, Armonk, New York) to compute differences in demographic, clinical, and measured variables. A Bonferroni correction for multiple comparison was used when necessary.

Results

The characteristics of our subjects are shown in Table 1. The re-CPAP group was slightly older and heavier than the control group. The mean age at the first CPAP initiation in the re-CPAP group was 57.8 y, mean body mass index was 34.8 kg/m², and mean respiratory event index was 39.4 events/h.

RESTARTING CPAP AFTER PREVIOUS FAILURE

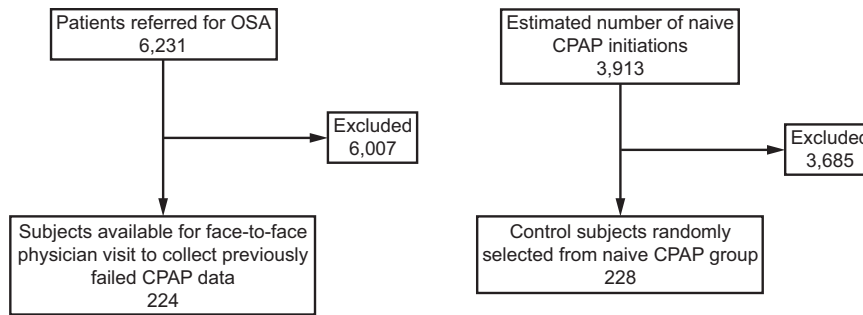


Fig. 1. Flow chart. OSA = obstructive sleep apnea.

Table 1. Subject Characteristics

	Re-CPAP Group	Control Group	<i>P</i>
Age, y	57.8 ± 11.0	55.0 ± 13.5	.02
Body mass index, kg/m ²	34.8 ± 10.2	31.6 ± 7.0	.001
Epworth sleepiness scale at baseline	9.5 ± 5.4	9.1 ± 5.1	.35
Epworth sleepiness scale with CPAP	7.8 ± 5.1	6.4 ± 4.0	.01
Respiratory event index, events/h	39.4 ± 24.4	32.6 ± 22.2	.01
Oxygen desaturation index at 4% threshold	36.8 ± 25.8	32.3 ± 21.9	.17
S _{pO₂} , %	92.2 ± 3.1	92.2 ± 2.7	.55
CPAP duration, d	483.2 ± 763.9	357.2 ± 246.9	.01
CPAP daily use, hh:min	2:37 ± 2:19	3:58 ± 2:46	< .001
Apnea-hypopnea index with CPAP	5.0 ± 7.0	2.8 ± 4.5	< .001
Leak median, L/min	4.8 ± 7.9	5.2 ± 10.0	.76
Leak 95th, L/min	18.3 ± 12.7	18.5 ± 13.8	.21
Humidification, %	81.7	99.1	< .001
UPP, %	6.3	1.3	.005

Data are presented as mean ± SD. *P* values were determined with 2-tailed *t* tests. Re-CPAP = re-initiation of CPAP; UPP = uvulopalatopharyngoplasty.

The mean age, body mass index, respiratory event index at baseline, and the percentage with previous uvulopalatopharyngoplasty for the re-CPAP group was higher than that of control group (Table 1). No significant differences were observed regarding ESS, oxygen desaturation index at 4% threshold, or S_{pO₂} values between the re-CPAP and control groups. With CPAP therapy, values of ESS, median leak, and leak 95th did not differ significantly between re-CPAP and control groups; CPAP daily use (in hours:minutes) was significantly lower in the re-CPAP group than in the control group (2:37 vs 3:58, *P* < .001) (Table 1). Humidification was used in 81.7% of the re-CPAP group versus 99.1% of the control group (*P* < .001).

The prevalence of comorbidities was significantly higher in the re-CPAP group than in the control group. These comorbidities include asthma, COPD, heart arrhythmia, high blood pressure, diabetes mellitus, and coronary heart disease. We found no significant difference in abandoning CPAP therapy in relation to the following comorbidities: asthma, psychiatric disease, COPD, diabetes mellitus, heart arrhythmia, or hypertension. Subjects with coronary heart

disease had a greater tendency to abandon CPAP therapy in both the re-CPAP group and the control group (chi-square [1, *n* = 206] = 8.418, *P* = .006) (Table 2).

CPAP therapy was re-initiated after a mean lapse time of 5.2 y from the first initiation. During the time lapse, body mass index increased significantly from 32.6 to 38.8 kg/m², reflecting a weight gain of 1.5 kg/y for a person of 175 cm. The outcome of CPAP re-initiation was not related to the lapse time (Fig. 2). The mean follow-up period of the re-CPAP group was 483 d (range, 1 d to 11 y); the mean follow-up period of the control group was 357 d (*P* = .01).

For the re-CPAP group, 52% were still on CPAP therapy after a mean period of 483 d. For the control group, 67% were still on CPAP after a mean period of 357 d. Because the follow-up period differed between the 2 groups, we re-calculated the CPAP success rate. In our previous publication,¹² we reported that 2.8% of subjects abandoned CPAP therapy yearly. When the follow-up period of the re-CPAP group was adjusted to that of the control group, 66% of the subjects in the re-CPAP group stayed on CPAP (Fig. 3).

RESTARTING CPAP AFTER PREVIOUS FAILURE

We did not find a significant difference in the number of subjects still on CPAP between men in the re-CPAP group and men in the control group. However, this difference was statistically significant for women ($P = .002$) (Fig. 4). CPAP re-initiation therapy failed significantly more often

Table 2. Prevalence of Comorbidities

	Re-CPAP Group	Control Group	<i>P</i>
Asthma	30 (28)	32 (14)	.004
COPD	12 (12)	10 (5)	.02
Heart arrhythmia	21 (21)	27 (12)	.043
Hypertension	72 (66)	107 (48)	.002
Psychiatric disorders	56 (51)	56 (25)	< .001
Diabetes mellitus	51 (45)	40 (18)	< .001
Coronary heart disease	18 (18)	18 (8)	.01

Data are presented as *n* (%).

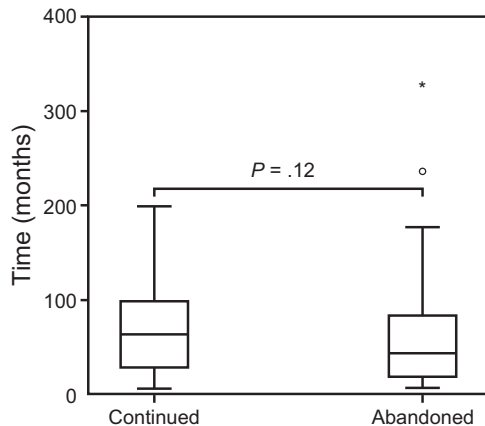


Fig. 2. Outcomes of CPAP re-initiation related to elapsed time since previous failure. Point and asterisk show outlier and extreme outlier, respectively.

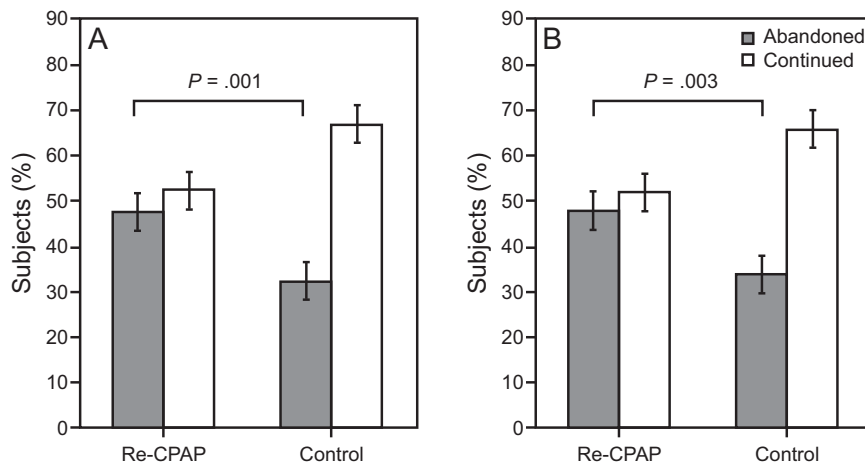


Fig. 3. A: Percentage of subjects continuing or abandoning CPAP therapy in the CPAP re-initiation (re-CPAP) and control group. B: Values adjusted for the follow-up period of the re-CPAP group.

in women than in men (62% vs 40%, $P = .002$). The likelihood ratio of staying on CPAP when re-initiated between men and women was 6.8, meaning that women were 6.8 times less likely than men to stay on CPAP therapy after a previous failure.

Because the women were older than the men, we examined whether this gender difference was related to age. In women, abandoning CPAP therapy did not correlate with age ($r = 0.086$, $P = .068$). Subjects who continued CPAP therapy after re-initiation had significantly higher baseline ESS and ESS CPAP values (in both men and women) than did subjects who abandoned CPAP therapy. No differences in body mass index or age were observed. The mean duration (hours:minutes) of daily CPAP use was significantly higher in the control group (3:58) than in the re-CPAP group (2:37) ($P < .001$).

Discussion

In this study, we observed that a previous failure in CPAP therapy constituted a risk factor for subsequent CPAP therapy failure. In the control group, 33% of subjects abandoned their therapy within 1 y, whereas the failure rate was 48% in the group of subjects with a previous failure.

Compared to men, women achieved success with CPAP re-initiation less frequently than the control group. We also observed no difference in CPAP adherence at CPAP initiation for the first time, which is consistent with a previous study.¹³ The difference in adherence at re-initiation may be related to the way men and women approach CPAP therapy. Previous studies on relapses in smoking-cessation trials reported that women were more likely than men to transition from being a former smoker to a current smoker.¹⁴ Further studies are needed to clarify the higher rate of CPAP re-initiation failure in women.

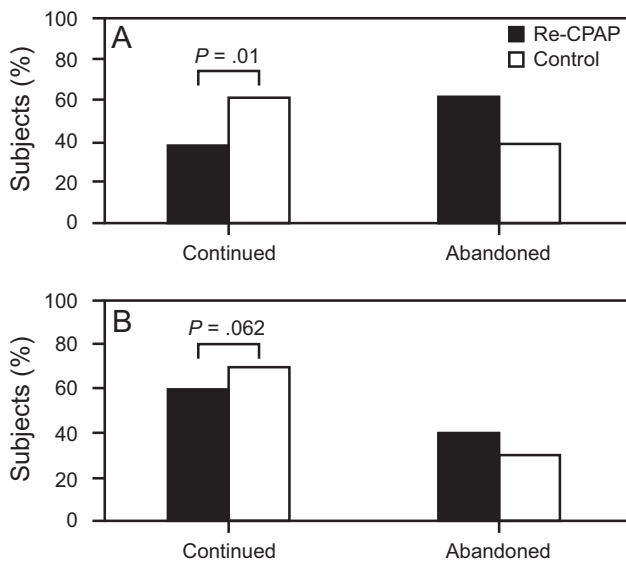


Fig. 4. Percentage of (A) women and (B) men continuing or abandoning CPAP therapy after 1 year.

In many cultures, snoring is generally considered a masculine trait. In addition, women with sleep apnea use health care services more often than men, and the prevalence of anxiety and depression is higher in women with sleep apnea than in men.^{15,16} We therefore hypothesize that when women accept a CPAP trial, they are more invested in their therapy than men are at their first trial.

In our population, the women were slightly older than men but this did not explain our results because staying on CPAP therapy did not correlate with age, consistent with a previous study.¹⁷ The success of CPAP therapy was reported to be higher in subjects with a higher respiratory event index, although adherence to CPAP therapy was significantly lower in the re-CPAP group than in the control group. Although humidification is known to reduce the side effects of CPAP therapy,¹⁸ the effect of humidification on CPAP adherence is still controversial.¹⁹ The first humidification devices were costly and bulky, and therefore their use was limited. Early advancements in mask comfort or CPAP device characteristics did not considerably affect therapy adherence.⁷ We believe that mask interfaces are currently more suitable and comfortable, and this may affect CPAP outcomes.

A previous uvulopalatopharyngoplasty has been reported as a risk factor for CPAP failure.²⁰ We believe that uvulopalatopharyngoplasty may have played a minor role in compromising the success of re-initiation of CPAP, given that its prevalence in our subjects was only 6.3%. We observed a higher prevalence of comorbidities in the re-CPAP group than in the control group, likely because these subjects did not use any effective sleep apnea therapy for a period of time. The prevalence of comorbidities did not

influence the success of CPAP therapy. One exception was sleep apnea subjects also suffering from coronary heart disease. These subjects abandoned CPAP therapy significantly more often than those without coronary heart disease. We did not find publications in the literature to support this finding. Despite the availability of the CPAP device in Finland, we still observed differences between men and women. This leads us to believe that economic considerations of the therapy do not play a significant role in CPAP adherence.

Our study has some limitations. This was a single-center study, so we cannot generalize our results to other centers. We defined a minimum period of 6 months between discontinuing CPAP therapy and re-initiation for the inclusion of subjects with CPAP failure. This time period was not supported by the literature because this subject has not been previously studied. The definition of CPAP failure was that the subject abandoned CPAP therapy and returned the CPAP device to the hospital. Some patients keep the device at home but rarely use it. We previously described that CPAP therapy in Finland is fully subsidized by public health insurance.¹⁰ This may suggest that patients are willing to re-initiate CPAP therapy after previous failure with a lower degree of motivation than if the therapy were not fully insured. No data on CPAP pressure levels were reported. We did not address the potential causes of CPAP failure, such as complex sleep apnea. We also did not evaluate other therapeutic ventilation modes. Finally, we did not evaluate or report the subject's psychologic profile, which may affect CPAP adherence as recently described.²¹

Conclusions

Although the probability of success after a previous CPAP therapy failure was lower than in the control group, more than half of these patients stayed on CPAP therapy after re-initiation. The success of CPAP re-initiation is lower in women than in men, so women may require closer follow-up and intervention to adhere to CPAP therapy.

REFERENCES

1. Bachour A, Maasilta P. Mouth breathing compromises adherence to nasal continuous positive airway pressure therapy. *Chest* 2004;126(4):1248-1254.
2. Kotecha BT, Hall AC. Role of surgery in adult obstructive sleep apnoea. *Sleep Med Rev* 2014;18(5):405-413.
3. Palotie T, Riekkio S, Mäkitie A, Bachour A, Arte S, Bäck L. The effect of mandible advancement splints in mild, moderate, and severe obstructive sleep apnea—the need for sleep registrations during follow up. *Eur J Orthod* 2017;39(5):497-501.
4. Kompelli AR, Ni JS, Nguyen SA, Lentsch EJ, Neskey DM, Meyer TA. The outcomes of hypoglossal nerve stimulation in the management of OSA: a systematic review and meta-analysis. *World J Otorhinolaryngol Head Neck Surg* 2019;5(1):41-48.
5. Aloia MS. Identifying moderators of CPAP efficacy. *Sleep* 2011;34(1):9-10.

6. Bachour A, Virkkala J, Maasilta P. AutoCPAP initiation at home: optimal trial duration and cost-effectiveness. *Sleep Med* 2007;8(7-8):704-710.
7. Berry RB. Improving CPAP compliance – man more than machine. *Sleep Med* 2000;1(3):175-178.
8. Koivumäki V, Maasilta P, Bachour A. Oximetry monitoring recommended during PAP initiation for sleep apnea in patients with obesity or nocturnal hypoxemia. *J Clin Sleep Med* 2018;14(11):1859-1863.
9. Kreivi HR, Maasilta P, Bachour A. Willingness score obtained after a short CPAP trial predicts CPAP use at 1 year. *Sleep Breath* 2014;18(1):207-213.
10. Avellan-Hietanen H, Brander P, Bachour A. Symptoms during CPAP therapy are the major reason for contacting the sleep unit between two routine contacts. *J Clin Sleep Med* 2019;15(1):47-53.
11. Working group set up by Duodecim, The Finnish Pulmonary Doctor's Association and the Finnish Unitutkimusseura ry. Sleep apnea: current care guidelines. Available at: <https://www.kaypahoito.fi/hoi50088>. Accessed June 29, 2020.
12. Bachour A, Vitikainen P, Maasilta P. Rates of initial acceptance of PAP masks and outcomes of mask switching. *Sleep Breath* 2016;20(2):733-738.
13. Aro M, Anttalainen U, Kurki S, Irjala K, Polo O, Saaresranta T. Gender-specific change in leptin concentrations during long-term CPAP therapy. *Sleep Breath* 2020;24(1):191-199.
14. Smith PH, Bessette AJ, Weinberger AH, Sheffer CE, McKee SA. Sex/gender differences in smoking cessation: a review. *Prev Med* 2016;92:135-140.
15. Ye L, Pien GW, Weaver TE. Gender differences in clinical manifestations of obstructive sleep apnea. *Sleep Med* 2009;10(10):1075-1084.
16. Cairns A, Poulos G, Bogan R. Sex differences in sleep apnea predictors and out-comes from home sleep apnea testing. *Nat Sci Sleep* 2016;8:197-205.
17. Turnbull CD, Bratton DJ, Craig SE, Kohler M, Stradling JR. In patients with minimally symptomatic OSA can baseline characteristics and early patterns of CPAP usage predict those who are likely to be longer-term users of CPAP. *J Thorac Dis* 2016;8(2):276-281.
18. Kreivi HR, Maasilta P, Bachour A. Persistence of upper-airway symptoms during CPAP compromises adherence at 1 year. *Respir Care* 2016;61(5):652-657.
19. Zhu D, Wu M, Cao Y, Lin S, Xuan N, Zhu C, et al. Heated humidification did not improve compliance of positive airway pressure and subjective daytime sleepiness in obstructive sleep apnea syndrome: a meta-analysis. *PLoS One* 2018;13(12):e0207994.
20. Mortimore IL, Bradley PA, Murray JA, Douglas NJ. Uvulopalatopharyngoplasty may compromise nasal CPAP therapy in sleep apnea syndrome. *Am J Respir Crit Care Med* 1996;154(6):1759-1762.
21. Broström A, Strömberg A, Mårtensson J, Ulander M, Harder L, Svanborg E. Impact of type D personality on adherence to oral appliance therapy for sleep-disordered breathing. *J Sleep Res* 2007;16(4):439-447.