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Short-Term Usage Time and Rate of CPAP Predict Long-Term CPAP Adherence in Patients with Obstructive Sleep Apnea

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Abstract

Objective: Obstructive sleep apnea (OSA) is a highly prevalent disease associated with various morbidities worldwide. Although continuous positive airway pressure (CPAP) is the cornerstone of therapy, adherence to CPAP directly affects its efficacy.

Methods: We retrospectively investigated consecutive patients who were diagnosed with OSA and placed on CPAP therapy within an approximate ten-year period. Using patient characteristics and short-term usage, the predictors of adherence to CPAP were evaluated.

Results: Overall, 234 patients were included (median follow-up, 45.4 months; median age, 59 years; and apnea-hypopnea index, 44.7 per hour). One half was classified as the minimally symptomatic phenotype. Short-term evaluations were performed after a median of 8 days after treatment initiation. CPAP was continued in 60.7% patients and the estimated 5-/10-year continuation rate of CPAP was 64.8% (95% confidence interval (CI): 57.8-70.9) and 50.0% (95% CI: 41.2-58.1), respectively. In a multivariable Cox proportional hazard model, age, short-term usage time and use rate of CPAP were identified as the predictors of adherence. The threshold values of usage time and use rate were 3 hours per night and 80%, respectively. When categorizing whether both values were fulfilled, the long-term adherence were divided significantly.

Conclusions: Short-term adherence to CPAP for approximately one week predicts long-term adherence. Both usage time and rate are important in evaluating adherence. Earlier, intensive interventions for patients who do not have a short-term usage time of at least 3 hours per night and use rate of 80% in even very short period may improve long-term CPAP adherence. (247 words)

Keywords: Obstructive Sleep Apnea; CPAP; Adherence; Predictor

List of abbreviations:

OSA: Obstructive Sleep Apnea; CPAP: Continuous Positive Airway Pressure; AHI: Apnea-Hypopnea Index; ODI: Oxygen Desaturation Index; CI: Confidence Interval

Introduction

Obstructive sleep apnea (OSA) is one of the most common diseases worldwide. Among adults aged 30–69 years, 936 million have an apnea-hypopnea index (AHI) of 5 or more and 425 million adults have an AHI of 15 or more [1]. The cornerstone of therapy for moderate and severe OSA is continuous positive airway pressure (CPAP). CPAP is effective in treating not only OSA-specific issues, such as the reduction of AHI or improvement of excessive daytime sleepiness, but can also reduce cardiovascular disease [2] and cardiovascular death [3] as well as contribute to the improvement of social issues, such as traffic accidents [4]. The effectiveness of CPAP is considered usage-time dependent [5]; normalization of cardiovascular risk, subjective sleepiness, objective sleepiness, memory, and daily function are found to require CPAP usage more than 4, 4, 6, 6 and 7.5 hours per night, respectively [6]. Because the interruption of CPAP therapy after only a few days results in the loss of effectiveness [7], the continuation of good adherence is also necessary. To date, CPAP use of 4 hours per night on 70% of nights has been generally established as a clinical and empiric benchmark of adherence [5,8,9].

In practice, CPAP adherence decreases with time, especially within 3 months after initiation [10-12], meaning that long-term adherence is suboptimal, and reported nonadherence ranges from 29-83% depending on follow-up duration [13-16]. However, it is difficult to continue interventions to maintain good adherence in all patients because of the high prevalence of OSA. Therefore, intensive intervention is desirable for patients who are predicted, in the early stages of treatment, to become nonadherent. Thus, in this study, we investigated the predictors of long-term continuation to CPAP therapy using commonly obtained factors in usual care settings immediately after CPAP initiation.

Methods

Patients: Consecutive patients diagnosed with OSA by in-hospital polysomnography and who initiated CPAP at Komaki City Hospital between March 2010 and November 2021 were retrospectively evaluated. This study was approved by the Institutional Review Board (No. 211028). The requirement for informed consent was waived because of the retrospective nature of the study. All data were dealt as anonymized. The indication for CPAP was based on the arbitrary criteria of the Japanese Ministry of Health, Labor and Welfare: clinical OSA with an AHI of 20 or more [17].

Applications: CPAP was directly applied to each patient at home by experienced home care providers, and the first visit, usually one to two weeks later, was followed by monthly visits by a specialized doctor. Monthly evaluation of CPAP therapy was done by considering self-reported usage, symptom and CPAP data from built-in recorder. The Auto Set C, Air Sense 9 or 10 system (ResMed Co., San Diego, CA, USA) was used as the CPAP machine, and all patients were initially administered CPAP setting auto-PAP to 4 to 12 cmH2O and via a nasal mask. Home care providers addressed the consultation about CPAP machine, and doctors and nurses managed the mask-fitting and the side effects. If necessary, type of mask or PAP level was modified and humidifier or topical treatment was applied.

Data collection: Patient characteristics, age, sex, comorbidities relevant to OSA, smoking history, body mass index, Epworth sleepiness scale, Pittsburgh Sleep Quality Index, and phenotype of subjective symptoms were recorded. Based on the classification reported by Ye et al. [18], two experienced doctors independently assigned each phenotype and, if unmatched the phenotype of the same patient, discussed and decided one phenotype. Sleep efficacy, arousal index, respiratory arousal index, AHI, apnea index, oxygen desaturation index (ODI), positional OSA, and snoring rate were recorded as the PSG data. In the short-term evaluation, the use rate (days), daily usage time (hours), 95th percentile leak (L/min), and residual AHI were recorded. Long-term adherence was evaluated by medical records or remote monitoring of the CPAP built-in recorder (final access in November 2022). We investigated CPAP continuation, defined as using the CPAP machine, and good adherence (usage time of 4 hours per night or more and use rate of 70% or more [5] during the last month) as the outcomes.

Statistics: The baseline characteristics were shown as median (interquartile range), and chi square test and Mann-Whitney U test were used to compare between groups as appropriate. Utilizations were analyzed using Kaplan–Meier curves, and comparisons were performed using the log-rank test. The predictors were extracted using a multivariable Cox proportional hazard model including the significant factors from univariate analyses performed on all each independent variables. The threshold values of the predictors were determined using the receiver operating characteristic (ROC) curve. All statistical analyses were performed using SPSS ver. 23 (IBM, Armonk, NY, USA) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). A p-value < 5% was considered significant.

Results

Over the ten-year study period, 248 patients were diagnosed with OSA, and CPAP treatment was initiated in our institute. After the exclusion of 10 patients without short-term evaluation or long-term clinical information and 4 patients who died or were no longer receiving CPAP because of other diseases, a total of 234 patients were included (Figure 1). Patient characteristics are shown in Table 1, with a median age of 59 years and AHI of 44.7 per hour, and predominantly male. The interobserver consistency of the phenotype was moderate (k=0.767, 95% confidence interval [CI]: 0.729-0.805), and one half was classified as the minimally symptomatic phenotype. The short-term evaluation was performed a median of 8 days after CPAP initiation, with a median usage time of 4.5 hours per night and use rate of 93%. The usage of nine patients who abandoned before the first visit was recorded as 0 hour per night and use rate of 0%.

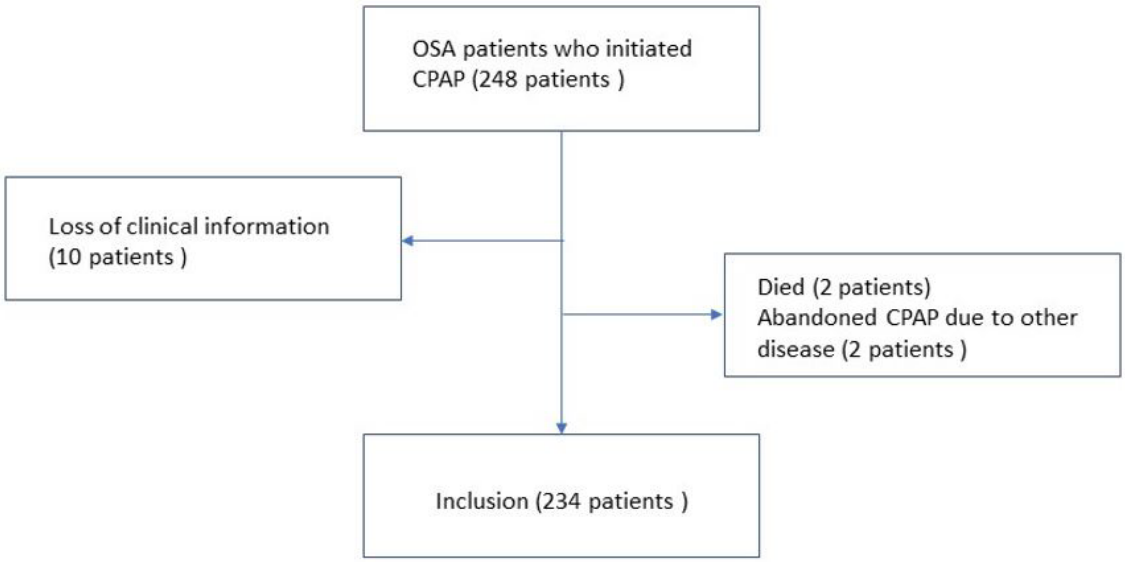

Figure 1: Flowchart of study population

Table 1: Patient characteristics

	Total	CPAP adherant	CPAP abandont	p value
Background				
Gender (M/F)	203/31	124/18	79/13	0.844
Age #	59 (48-69)	57.5 (51-71)	57.5 (46.5-67.5)	0.030
Body mass index #	27.7 (24.6-30.4)	28.1 (24.9-30.7)	27.0 (23.6-29.4)	0.070
Smoking history (y/n)	135/71	82/49	53/22	0.154
Comorbidity (N(%))				
None	54 (23.1)	30 (21.1)	24 (26.1)	0.235
Cardiovascular disease	61 (26.1)	35 (15.0)	26 (28.3)	0.330
Hypertension	98 (41.9)	63 (26.9)	35 (38.0)	0.206
Other	98 (41.9)	60 (25.6)	38 (41.3)	0.893
Epworth sleepiness score #	8 (5-11)	8 (5-11)	8 (4-11)	0.676
PSQI #	6 (4-8)	7.5 (4-8.5)	6 (6-7)	0.968
Phenotype (N(%))				0.385
Minimally symptomatic	121 (51.7)	69 (48.6)	52 (56.5)	
Excessive daytime sleepiness	92 (39.3)	58 (40.8)	34 (37.0)	
Disturbed sleep	21 (9.0)	15 (10.6)	6 (6.5)	
PSG data				
Sleep efficacy rate (%)#	73.6 (63.3-85.3)	73.8 (66.2-85.6)	72.9 (58.3-84.6)	0.353
Arousal index (/h)#	37.4 (28.8-48.8)	38.8 (30.0-50.0)	36.1 (27.5-45.3)	0.082
Respiratory arousal index (/h)#	24.3 (11.2-37.4)	25.3 (13.4-38.5)	21.3 (9.9-35.2)	0.095
AHI (/h)#	44.7 (33.7-56.7)	46.0 (35.8-58.7)	41.8 (30.5-54.3)	0.058
Apnea index (/h)#	22.7 (10.9-41.0)	24.1 (11.9-42.4)	19.3 (9.5-32.9)	0.106
Obstructive apnea index (/h)#	18.2 (9.5-33.0)	20.9 (10.6-41.1)	17.5 (8.8-30.6)	0.315
Central apnea index (/h)#	0.0 (0.0-0.6)	0.0 (0.0-0.7)	0.0 (0.0-0.4)	0.546
Positional sleep apnea (N(%))	139 (59.4)	78 (54.9)	61 (66.3)	0.055
Oxygen desaturation index (/h)#	41.2 (28.4-55.8)	42.3 (29.6-57.0)	40.4 (27.7-52.0)	0.426
Snoring rate (%)#	9.4 (4.0-19.3)	10.6 (4.3-20.3)	8.6 (3.6-16.1)	0.172
Short-term usage				
Days after initiation #	8 (6-12)	8 (6-12)	8.5 (6-12.5)	0.442
Usage time (h/d)#	4.5 (2.9-6.0)	4.9 (3.4-6.2)	4.1 (1.4-5.5)	0.007
Use rate (%)#	93 (55-100)	100 (83-100)	88 (50-100)	0.001
PAP (mmHg)#	7.9 (6.7-9.5)	7.8 (6.7-9.2)	8.0 (6.7-9.7)	0.420
Mask leak (95% value, L/min)#	0.2 (0.1-0.4)	0.2 (0.1-0.4)	0.2 (0.1-0.5)	0.420
Residual AHI (/h)#	2.2 (1.1-4.3)	2.3 (1.2-4.0)	2.1 (1.1-5.2)	0.848

median (interquartile range), PSQI: Pittsburgh Sleep Quality Index,

AHI: apnea-hypopnea index, PAP: positive airway pressure

CPAP was continued in 60.7% (95% CI: 54.1-67.0) patients, with a median follow-up of 45.4 months. Among those patients, the good adherence was achieved in 56.3% (95% CI: 47.8-64.6) of patients. The estimated continuation rates for 1 / 5 / 10-years were 79.6% (95% CI: 73.8-84.3) / 64.8% (95% CI: 57.8-70.9) / 50.0% (95% CI: 41.2-58.1), respectively (Figure 2). Using patient characteristics and short-term evaluation by the multivariable Cox proportional hazard model, age, short-term usage time and use rate were extracted as predictors of CPAP adherence (Table 2). The phenotype was not related to long-term adherence.

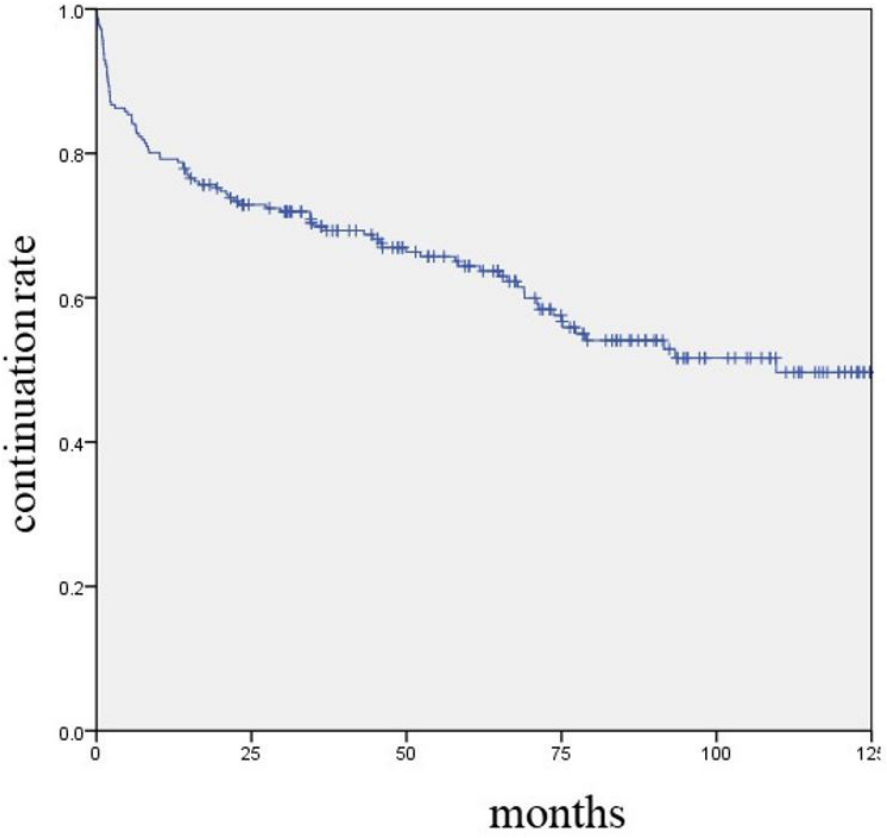

Figure 2: Kaplan-Meier analysis of CPAP adherence

Table 2: Predictors of CPAP adherence extracted by univariable and multivariable Cox proportional hazard model

	Univariable			Multivariable		
	HR	95% CI	p value	HR	95% CI	p value
Age	1.017	1.000-1.033	0.049	1.029	1.012-1.047	0.001
AHI	0.986	0.974-0.999	0.030	0.987	0.974-1.000	0.054
Use rate	0.982	0.975-0.988	<0.001	0.986	0.977-0.995	0.004
Usage time	0.794	0.720-0.876	<0.001	0.852	0.747-0.971	0.016

HR: hazard ratio, CI: confidence interval, AHI: apnea-hypopnea index

A moderate correlation between usage time and use rate was revealed in the short-term and long-term evaluations (Spearman's rank correlation; r = 0.664 (p<0.001) and 0.692 (p<0.001), respectively). The contribution rates of both predictors together were 9.4% for long-term CPAP adherence. Moreover, using ROC curve, the best threshold values for long-term CPAP adherence to short-term usage time and use rate were 2.90 hours per night and 81.2%, respectively (aera under the curve was 0.624 and 0.599, respectively). When categorizing whether both criteria (namely, usage time of 3 hours or more and use rate of 80% or more in short-term evaluation) were fulfilled, the long-term adherence were divided significantly (log rank test; p<0.001) (Figure 3).

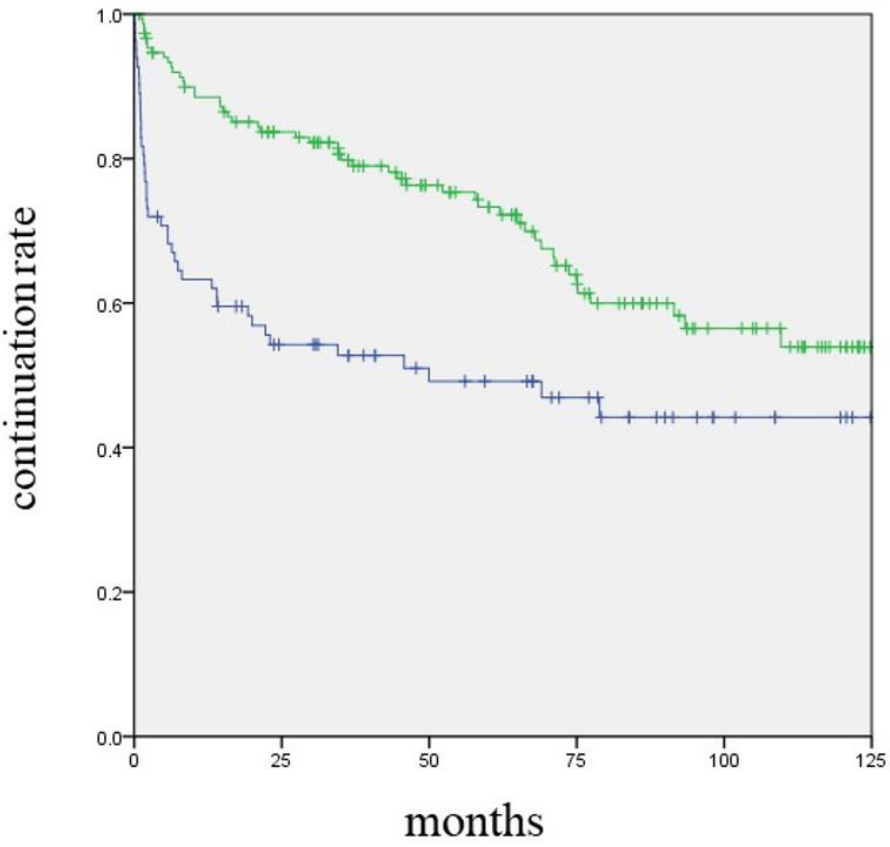

Figure 3: Kaplan–Meier analysis of CPAP adherence divided by short-term usage

The green/blue line shows patients with or without good short-term usage, respectively. A significant difference between the two curves was detected using the log rank test ($p<0.001$)

Discussion

We extracted the predictors of long-term CPAP adherence using factors commonly obtained in usual care settings immediately after CPAP initiation. Usage time and use rate after one week following initiation were significant predictors of adherence after a median follow-up of 45 months. Short-term usage time of 3 hours per night or more and use rate of 80% or more was the threshold value for long-term adherence. In cases under these thresholds in the early period, intensively investigating and solving the cause of nonadherence may prevent CPAP abandonment and contribute to good adherence.

Although many predictors of adherence have been studied, no reliable predictor has yet been identified. Among the patient factors, OSA severity (AHI or ODI), excessive daytime sleepiness, reduced volume of the nasal cavity, claustrophobia, and active coping styles are relevant to CPAP adherence; whereas age, character, cognitive perception of OSA, depression, and low mood seem to be inconsistent. In terms of medical care, auto positive airway pressure and supportive introduction are useful for adherence, and complications induced by CPAP, use of humidifiers, or type of mask do not affect adherence [8-10,13,19]. Because the investigated factors are different in each study and the reported predictors can affect adherence in only 4 - 25% [19,20], it is difficult to identify reliable long-term predictors with multifaced features.

Moreover, no feasible methods to improve adherence have been established, and no improvement in adherence has been detected in the last 30 years [21]. Long-term adherence is affected by both multifaceted and highly individualized factors; therefore, patients require individual evaluation and support. Recently, telemedicine, involving remote monitoring or supportive care using the telephone, has been reported to be useful in improving CPAP adherence. Although its efficacy has been validated [22], a standard method still needs to be established.

In this study, usage time and rate of CPAP in the short term could predict long-term adherence to CPAP therapy. Although short-term adherence has been previously reported to predict long-term adherence [16,20,23-29], few studies have evaluated both usage time and use rate as predictors of long-term adherence [15,27,30]. In a review of CPAP adherence in 82 articles, the nonuse rate was suboptimal, describing 10 - 40%, compared to fair usage time of 4.6 hours per night [21]. Furthermore, the correlation between usage time and rate was not sufficient in this study, similar to other study [24]. When evaluating of CPAP efficacy having the time dependency [5], the use rate should be considered separately in addition to usage time.

In most previous studies, short-term evaluation was performed between 3 days and one month after the initiation of CPAP therapy [20,24-29]. Evaluation performed too early can reduce the reproducibility of the results, while if the evaluation is performed too late, some patients may have already abandoned CPAP. Indeed, very early abandonment of CPAP (within one week) occurs in 4 to 16 % of all patients [10,12,20,27]. Considering the early formation of adherence to CPAP [10,13], approximately one week was deemed a reasonable duration for short-term evaluation. Regarding follow-up duration, although most studies investigated long-term usage 3 to 6 months later [23-25,27,29], with the longest duration of about two years [16,20], we could confirm the more long-term effect of short-term adherence in a much longer duration.

Several studies have investigated after ruling out the patients with very early abandonment in a CPAP trial of one to two weeks [12,16,26]. In practice, such patients need to be managed; therefore, we included all patients initiating CPAP to extract the predictors.

Our study had several limitations. First, this study was performed at a single institution. Although this might introduce bias, this would have allowed uniformity in the initiation and management of CPAP therapy, including CPAP devices and masks. Second, the retrospective design and small sample size may cause statistical underpower; therefore, a prospective validation study with a larger cohort is warranted, or the utility of early intervention based on our predictors should be confirmed. Finally, the examined factors were insufficient because other factors reported as relevant, such as social or psychological, were not included. However, our predictors have the advantages of easy collection and simple interpretation in routine care.

Conclusions

In this study, the usage time and rate after approximately one week of CPAP initiation predicted long-term adherence after a median of 45 months. In the evaluation of adherence, we found that both usage time and use rate were important factors. Unless a usage time of 3 hours per night or more and a use rate of 80% or more even in very early period, the intensive investigation and intervention for the cause of nonadherence may contribute to long-term CPAP adherence.

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