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Original Article

Should sleep laboratories have their own predictive formulas for continuous positive airway pressure for patients with obstructive sleep apnea syndrome?

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Abstract

Background: Several formulas predicting optimal continuous positive airway pressure (CPAP) for obstructive sleep apnea treatment have been developed and diverse parameters selected as predictive factors in different sleep laboratories using different ethnic groups. This study aimed to validate a constructed predictive formula for the study laboratory and to test the hypothesis that sleep laboratories should have their own predictive formulas.
Methods: Fifty-seven adult subjects with obstructive sleep apnea syndrome (OSAS) were enrolled in the model-building set and underwent two polysomnography (PSG) studies to diagnose OSAS and titrate for optimal CPAP. A predictive formula, derived from anthropometric and polysomnographic variables, was validated together with two other predictive formulas in 30 subjects by comparing the mean predictive CPAP values, rates of successful prediction, and agreements.
Results: Regression analysis showed that apnea–hypopnea index (AHI), SaO_{2nadir} (nadir of arterial oxyhemoglobin saturation by pulse oximetry), and body mass index (BMI) strongly correlated with optimal CPAP. The derived predictive formula for the study laboratory was: CPAPpred (predictive CPAP) = 6.380 + 0.033 × AHI − 0.068 × SaO_{2nadir} + 0.171 × BMI (R^2 = 0.335, adjusted R^2 = 0.298). In Taiwan, different predictive formulas used by different sleep laboratories with different independent predictors led to similar mean predictive CPAP values to the mean observed optimal CPAP values, rates of successful prediction, and agreements with the observed optimal CPAP. There were significant differences between the mean predictive CPAP values and mean observed optimal CPAP values, lower rates of successful prediction, and negatively skewed 95% confidence interval (CI) when using a predictive formula derived from different ethnic populations.
Conclusion: A sleep laboratory may not need to have its own predictive formula for determining the optimal effective CPAP but should adopt the one derived from the same ethnicity of OSAS patients as the reference formula.

Keywords: continuous positive airway pressure; obstructive sleep apnea syndrome; predictive formula

1. Introduction

The social, legal, and economic impacts of obstructive sleep apnea syndrome (OSAS) have led to the rapid development of sleep medicine.[1] Continuous positive airway pressure (CPAP), first described in 1981 by Sullivan et al,[2] is the most effective therapy for patients with OSAS. Conventional

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manual, algorithm-based, and automatic positive airway pressure (APAP) titrations are the current available methods for determining therapeutic CPAP in patients with OSAS.

Conventional manual titration under attended polysomnography (PSG) remains the gold standard but is time-consuming and increases the PSG waiting list.[3] For simplicity, algorithm-based pressure is used, with favorable results.[4−6] It can be selected as the starting pressure at home, with subsequent adjustments. Similarly, APAP titration is more cost-effective than conventional manual titration, with the largest savings obtained when it is done at home.[7] It is therefore also considered an alternative for determining therapeutic CPAP.

Between algorithm-based titration and APAP titration, there is no study to date that has established better methods for obtaining effective CPAP. Both methods can effectively reduce daytime sleepiness, as evaluated by the Epworth questionnaire and apnea−hypopnea index (AHI).[8−10] However, there is poor agreement between the 95th percentile pressure obtained by APAP titration and the predictive pressure calculated by the algorithm-based titration, especially when the calculated pressures are <9 cmH_2O or >15 cmH_2O.[11,12]

APAP titration is contraindicated in certain medical conditions like congestive heart failure, chronic obstructive pulmonary disease, obesity hypoventilation syndrome, non-snorer, and central sleep apnea.[3,7] In addition, the required duration, the best algorithm and software, and the best particular derived pressure (i.e., 90th percentile, 95th percentile, etc.) of APAP all remain to be determined.[3] As such, APAP titration cannot replace algorithm-based titration despite the long waiting list for attended, full-night conventional manual titration.

Using different ethnic populations, several formulas to predict the observed optimal therapeutic CPAP (CPAPopt) (algorithm-based titration) have been developed over the past two decades. Miljeteig and Hoffstein[4] developed the first predictive formula using three independent predictors [body mass index (BMI), neck circumference (NC), and AHI] among Caucasians. In another Caucasian population, the prediction variables of the formula were smoking (pack/years), BMI, and AHI.[13] In Asians, Akahoshi et al[14] predicted CPAPopt using a combination of cephalometric, anthropometric (BMI), and polysomnographic (AHI and mean oxyhemoglobin saturation) data. In another Asian population, Lin et al[15] proposed a predictive formula using BMI and AHI as prediction variables, whereas BMI, AHI, and desaturation index were the prediction variables used by Chuang et al[16] in another Asian population. Thus, in different sleep laboratories, diverse parameters are selected as prediction variables even when using the same ethnic groups. However, it is necessary to determine if building a sleep laboratory's own predictive formula is better than adopting a predictive formula derived from another sleep laboratory as reference, or if adopting a predictive formula derived from the same ethnic group is better than using one based on a different ethnic group.

The aims of this study were (1) to construct and validate a CPAP prediction formula for a particular laboratory, and (2) to test the hypothesis that sleep laboratories should have their own predictive formulas.

2. Methods

2.1. Study participants

Fifty-seven adult subjects with OSAS [defined as AHI $\geq$5 events/hour, total sleep time (TST) $\geq$6 hours, sleep efficiency (SE) $\geq$70%] in Taichung Veterans General Hospital were enrolled sequentially from January 2007 to December 2008 and served as the model-building set. Thirty adult OSAS subjects were also enrolled from January 2009 to December 2009 to serve as the validation set. Subjects with major illnesses or under hypnotics were excluded. All enrolled subjects underwent at least two PSG studies. The first was to diagnose OSAS (diagnostic PSG) and the second was to determine the optimal CPAP (CPAP down titration). The hospital's Institutional Review Board and Ethics Committee approved this study.

2.2. Full-night diagnostic PSG

All subjects underwent a standard full-night diagnostic PSG (Compumedics, E-series, Victoria, Australia). Standard recordings included electro-encephalogram (EEG; C3/A2, C4/A1, O1/A2, and O2/A1), electro-oculogram (EOG), submental and tibialis anterior electro-myogram (EMG), electrocardiography (ECG), and measurements of oronasal airflow (simultaneously using a thermocouple), respiratory effort (using inductive plethysmography in the thorax and abdomen), arterial oxyhemoglobin saturation by pulse oximetry (SaO_2), and snoring (via small microphone attached around the cricoid cartilage). All data were manually scored based on the international criteria developed by Rechtschaffen and Kales to determine sleep/wakefulness, and the criteria developed by the Atlas Task Force of the American Sleep Disorders Association to determine arousal.[17,18]

The arousal index was defined as the number of arousal events divided by sleep time (hours) whereas the snore index was defined as the number of snore counts divided by sleep time. The apnea index (AI) was defined as the total number of apneas divided by the total sleep time (hours), whereas AHI was defined as the total number of apneas and hypopneas divided by the total sleep time. The severity of OSAS was graded as "mild" if AHI was 5−14, "moderate" if 15−30, and "severe" for >30 events per hour.

2.3. CPAP down-titration for optimal pressure

After orientation toward the function of nasal CPAP (GE Healthcare/Breas PV 100) and fitting of an appropriate-sized nasal mask to the subjects, the starting pressure was set as 4 cmH_2O. The CPAP was then raised by 0.5−1.0 cmH_2O every 5−15 minutes until all respiratory events, including apneas, hypopneas, arousals, transient desaturation, and snoring, were eliminated. The pressure level was then decreased by 0.5−1.0 cmH_2O every 5−15 minutes until any respiratory event reappeared. The pressure was again raised by 0.5−1.0 cmH_2O every 5−15 minutes until all respiratory events disappeared. The pressure level was held for at least 30 minutes and was

determined as the optimal CPAP.[19] At least 6 hours of sleep were allowed for the CPAP down-titration. Optimal CPAP was that which controlled all respiratory events while the subject was in the supine position and in rapid eye movement sleep.

2.4. Statistical analysis

For the model-building set, univariate regression analysis and Pearson's correlation were used to determine the bivariate relationship between CPAPopt and baseline data, including anthropometric and polysomnographic variables. Significant parameters, using those with larger R^2 first, were combined to determine the best-fit model to predict CPAPopt in terms of both accuracy and simplicity. Multivariate regression analysis was used to model the effect of selected significant variables and to develop a predictive formula for CPAPopt.

In the validation set, to compare the mean pressure differences of CPAP between the observed optimal CPAP and the pressures calculated by four predictive formulas, the Shapiro–Wilk test was used to check normality whereas the independent-sample t test or Mann–Whitney U test was used to analyze the mean pressure differences of CPAP. Bland–Altman Plot and 95% confidence interval (CI) were used to compare the agreement between CPAPopt and the pressures calculated by the three predictive formulas.

All data were presented as mean ± standard deviation (SD) for continuous variables and as frequencies (%) for categorical variables. Statistical analysis was performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

3. Results

Based on the anthropometric and polysomnographic data (Table 1), most of the subjects in both sets were obese and had severe OSAS. There were significant differences in several parameters, including age, TST, SE, AI, AHI, and arousal index.

In the model-building set, arousal index ($R^2 = 0.218$), AHI ($R^2 = 0.209$), SaO_{2nadir} ($R^2 = 0.191$), and BMI ($R^2 = 0.169$) significantly correlated with CPAPopt ($p < 0.01$). The NC ($R^2 = 0.093$) and AI ($R^2 = 0.082$) also significantly correlated with CPAPopt ($p < 0.05$; Table 2). By Pearson correlation analysis, there was a high correlation coefficient between arousal index and AHI ($r = 0.769$). As a result, two sets of parameters, one including AHI, SaO_{2nadir}, BMI, NC, and AI (Set 1) and the other including arousal index, SaO_{2nadir}, BMI, NC, and AI (Set 2), were included into the fit model.

For accuracy and simplicity, combinations of each set of parameters, with those with larger R^2 selected first, were assessed to build up the best-fit model for the study laboratory. Finally, a combination of three parameters—AHI, SaO_{2nadir}, and BMI in Set 1 and arousal index, SaO_{2nadir}, and BMI in Set 2—fulfilled both accuracy and simplicity, as determined by adjusted R^2 (Table 3). Multivariate regression analysis showed the final predictive models of the study laboratory as (Table 4):

$$\begin{aligned}\text{CPAPpred1} =& 6.380 + 0.033 \times \text{AHI} - 0.068 \\ & \times \text{SaO}_{2nadir} + 0.171 \times \text{BMI} \\ & \times \left(R^2 = 0.335,\ \text{adjusted}\, R^2 = 0.298\right)\end{aligned} \quad [1]$$

$$\begin{aligned}\text{CPAPpred2} =& 6.070 + 0.040 \times \text{arousal index} - 0.066 \\ & \times \text{SaO}_{2\text{nadir}} + 0.174 \times \text{BMI} \\ & \times \left(R^2 = 0.349,\ \text{adjusted}\, R^2 = 0.312\right)\end{aligned} \quad [2]$$

CPAPpred1 and CPAPpred2 denoted the predictive CPAP values by the study laboratory, CPAPeff denoted the value by Lin et al,[15] and CPAPmin the value by Miljeteig and Hoffstein.[4] In the validation set, the mean titrated CPAPopt values

Table 1
Anthropometric and polysomnographic data of enrolled subjects.

	Model-building set (n = 57; 52 male, 5 female)			Validation set (n = 30; 28 male, 2 female)			p
	Minimum	Maximum	Mean ± SD	Minimum	Maximum	Mean ± SD	
Age (y)	25	84	47.3 ± 11.25	28	84	53.3 ± 13.10	0.029[a,*]
TRT (h)	6.0	7.4	6.4 ± 0.37	5.9	7.2	6.3 ± 0.31	0.491[b]
TST (min)	279	440	356 ± 31.64	258	410	337.6 ± 37.13	0.017[a,*]
SE (%)	75	100	92.7 ± 6.41	71	99	88.6 ± 7.52	0.01[b,*]
AI (events/h)	0	70	16.9 ± 18.71	2	75	28.3 ± 18.76	0.001[b,**]
AHI (events/h)	14.4	84.1	46.4 ± 18.21	8	92	53.57 ± 18.34	0.044[b,*]
SaO_{2nadir} (%)	51	89	70.7 ± 9.36	51	87	71.9 ± 10.35	0.581[a]
Snore index (events/h)	0.9	2115.0	753.4 ± 606.66	22	2365	721.5 ± 552.66	0.945[b]
Arousal index (events/h)	7.9	78.9	42.2 ± 16.79	13	91	50.4 ± 19.04	0.04[a,*]
NC (cm)	35	47	41.2 ± 2.88	36	52	41.3 ± 3.32	0.781[b]
BMI	18.65	37.02	27.85 ± 3.44	23.03	35.86	28.11 ± 3.51	0.743[a]
CPAPopt (cmH_2O)	4.0	14.0	7.9 ± 2.38	4.0	13.0	8.4 ± 2.35	0.217[b]

*$p < 0.05$.
**$p < 0.01$.
AHI = apnea–hypopnea index; AI = apnea index; BMI = body mass index; CPAP = continuous positive airway pressure; CPAPopt = optimal CPAP pressure; CPAPpred = the predictive CPAP pressure; NC = neck circumference; SaO_{2nadir} = nadir of arterial oxyhemoglobin saturation by pulse oximetry; SD = standard deviation; SE = sleep efficiency; TRT = total recording time; TST = total sleep time.
[a] The p value was determined by independent-sample t test.
[b] The p value was determined by Mann–Whitney U test.

Table 2
Univariate regression analysis between CPAPopt and anthropometric and polysomnographic variables in the model-building set.

Parameters	β	R^2	Parameters	β	R^2	Parameters	β	R^2
Age	0.244	0.059	Arousal index	0.467	0.218**	NC	0.304	0.093*
TRT	0.068	0.005	AHI	0.457	0.209**	AI	0.286	0.082*
TST	0.124	0.015	SaO_2nadir	−0.437	0.191**	Snore index	0.024	0.001
SE (%)	0.082	0.007	BMI	0.411	0.169**			

*$p < 0.05$.
**$p < 0.01$.
AHI = apnea–hypopnea index; AI = apnea index; BMI = body mass index; CPAPopt = optimal continuous positive airway pressure; NC = neck circumference; SaO_{2nadir} = nadir of arterial oxyhemoglobin saturation by pulse oximetry; SE = sleep efficiency; TRT = total recording time; TST = total sleep time.

were compared with the mean CPAP values predicted by the formulas from this study and those by Lin et al[15] and Miljeteig and Hoffstein[4] (Fig. 1). Only the mean CPAP values predicted by Miljeteig and Hoffstein's[4] formula varied significantly from mean CPAPopt values ($p = 0.003$). Meanwhile, the mean CPAP values revealed no significant difference between CPAPpred1 and CPAPpred2.

In the validation set, using the predictive formula of the study laboratory, CPAPpred1, CPAPopt was within ±1 cmH_2O of CPAPpred1 in 30% (9/30), within ±2 cmH_2O in 56.7% (17/30), and within ±3 cmH_2O in 86.7% (26/30) of validated subjects. Using the predictive formula of the study laboratory, CPAPpred2, CPAPopt was within ±1 cmH_2O of CPAPeff in 30% (10/30), within ±2 cmH_2O in 63.3% (19/30), and within ±3 cmH_2O in 90% (27/30) of validated subjects. Using Lin et al's[15] formula (CPAPeff), CPAPopt was within ±1 cmH_2O of CPAPeff in 33.3% (10/30), within ±2 cmH_2O in 56.7% (17/30), and within ±3 cmH_2O in 80% (24/30) of validated subjects. Using Miljeteig and Hoffstein's[4] formula (CPAPmin), CPAPopt was within ±1 cmH_2O of CPAPmin in 20% (6/30), within ±2 cmH_2O in 46.7% (14/30), and within ±3 cmH_2O in 70.0% (21/30) of validated subjects (Fig. 2). These results indicated similar rates of successful prediction when applying the study laboratory's predictive formulas and Lin et al's[15] formula in various pressure differences, including ±1 cmH_2O, ±2 cmH_2O, and ±3 cmH_2O, which were higher than those when using Miljeteig and Hoffstein's[4] formula.

Based on both no significant difference of mean predicted CPAP values and similar rates of successful prediction between CPAPpred1 and CPAPpred2 and AHI being a strong predictor in previously published predictive formulas, the predictive formula, CPAPpred1, was selected to be the reference formula of the study laboratory.

In the validation set, assessing the agreement of the calculated pressures of the tested three predictive formulas with the observed optimal CPAP via Bland–Altman plot and 95% CI, there was a similar agreement in the three calculated pressures (CPAPpred1, 95% CI: −0.50–1.14; CPAPeff, 95% CI: −0.04–1.48; and CPAPmin, 95% CI: 0.70–2.30) with the observed optimal CPAP (Fig. 3). However, there was a negatively skewed 95% CI between CPAPopt and CPAPmin. This indicated that the tested three predictive formulas were interchangeable for the study laboratory.

Table 3
Assessment of the best-fit model for predicting CPAPopt in the model-building set.

Sets/ model	Parameters of predictor	Numbers of predictor	R^2	Adjusted R^2
Set 1				
1	AHI	1	0.209	0.194
2	AHI, SaO_{2nadir}	2	0.283	0.257
3	AHI, SaO_{2nadir}, BMI	3	0.335	0.298
4	AHI, SaO_{2nadir}, BMI, NC	4	0.336	0.285
5	AHI, SaO_{2nadir}, BMI, NC, AI	5	0.338	0.273
Set 2				
1	Arousal index	1	0.218	0.204
2	Arousal index, SaO_{2nadir}	2	0.294	0.268
3	Arousal index, SaO_{2nadir}, BMI	3	0.349	0.312
4	Arousal index, SaO_{2nadir}, BMI, NC	4	0.349	0.299
5	Arousal index, SaO_{2nadir}, BMI, NC, AI	5	0.352	0.289

AHI = apnea–hypopnea index; AI = apnea index; BMI = body mass index; CPAPopt = optimal continuous positive airway pressure; NC = neck circumference; SaO_{2nadir} = nadir of arterial oxyhemoglobin saturation by pulse oximetry.

4. Discussion

The present study shows that AHI, SaO_{2nadir}, and BMI are predictive factors for calculating CPAP values in the Taiwanese population in the study sleep laboratory. Among the

Table 4
Multivariate regression analysis for predicting CPAPopt.

	Nonstandardized coefficients		t	p	Collinearity statistics	
	B	Standard error			Tolerance	VIF
CPAPpred1						
(Constant)	6.380	3.555	1.795	0.078		
AHI	0.033	0.017	1.992	0.049*	0.758	1.319
SaO_{2nadir}	−0.068	0.032	−2.150	0.036*	0.817	1.226
BMI	0.171	0.084	2.040	0.046*	0.851	1.175
CPAPpred2						
(Constant)	6.070	3.529	1.720	0.091		
Arousal index	0.040	0.018	2.265	0.028**	0.790	1.266
SaO_{2nadir}	−0.066	0.031	−2.130	0.038**	0.825	1.213
BMI	0.174	0.082	2.111	0.040**	0.872	1.147

*$p < 0.05$; ANOVA $F = 8.917$; $R^2 = 0.335$; adjusted $R^2 = 0.298$.
**$p < 0.05$; ANOVA $F = 9.459$; $R^2 = 0.349$; adjusted $R^2 = 0.312$.
AHI = apnea–hypopnea index; ANOVA = analysis of variance; BMI = body mass index; CPAPopt = optimal continuous positive airway pressure; SaO_{2nadir} = nadir of arterial oxyhemoglobin saturation by pulse oximetry; VIF = variance inflation factor.

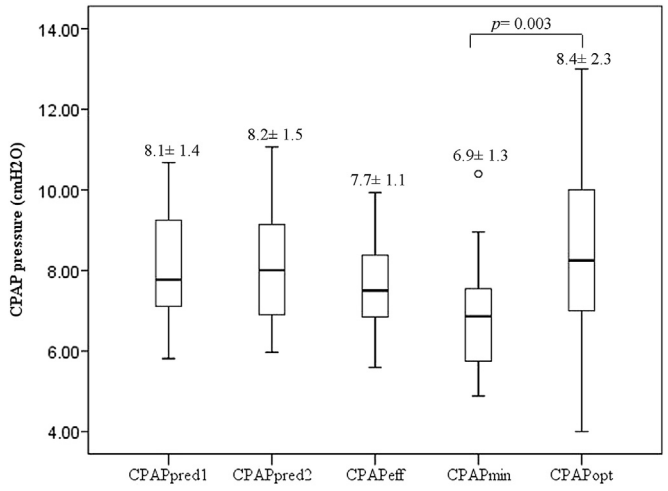

Fig. 1. Values (mean ± SD) of predictive CPAP using different predictive formulas in the validation set. Only mean CPAPmin values, not CPAPpred1, CPAPpred2, and CPAPeff, were significantly lower than that of CPAPopt. CPAP = continuous positive airway pressure; CPAPeff = predictive CPAP by Lin et al[15]; CPAPmin = predictive CPAP by Miljeteig and Hoffstein;[4] CPAPopt = observed optimal CPAP; CPAPpred = predictive CPAP by the current study; SD = standard deviation.

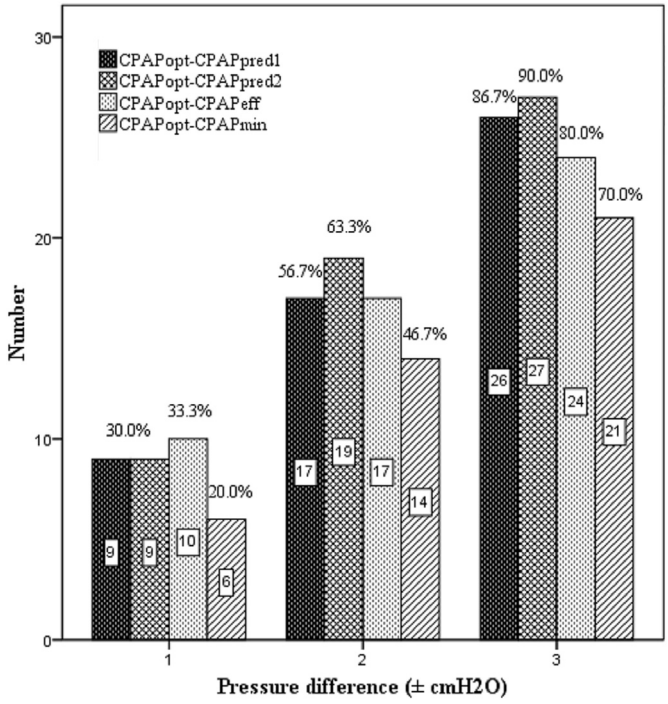

Fig. 2. Rates of successful prediction using various degrees of pressure difference (±1 cmH_2O, ±2 cmH_2O, and ±3 cmH_2O) between the observed optimal CPAP and the calculated CPAP via predictive formulas in the validated subjects. There were similar rates of successful prediction when applying the study laboratory's predictive formulas and the formula of Lin et al,[15] which were both higher than when applying the formula of Miljeteig and Hoffstein.[4] CPAP = continuous positive airway pressure; CPAPeff = predictive CPAP by Lin et al;[15] CPAPmin = predictive CPAP by Miljeteig and Hoffstein;[4] CPAPopt = observed optimal CPAP; CPAPpred = predictive CPAP by the current study; SD = standard deviation.

Taiwanese in different institutes, BMI and AHI have been adopted as independent predictors by Lin et al,[15] whereas Chuang et al[16] used BMI, AHI, and desaturation index. As such, different independent predictors have been adopted by different sleep laboratories for the same ethnic population. This may be because different sleep laboratories adopt different protocols for manual titration.

In the study sleep laboratory, down-titration has been used ever since manual titration began and is recommended due to the hysteresis phenomenon. This may result in lower optimal CPAP levels and better CPAP compliance.[20] Nevertheless, split-night PSG was adopted in Chuang et al's[16] sleep laboratory, although no illustration of the titration protocol was mentioned in Lin et al's[15] sleep laboratory.[15] The use of different protocols for manual titration may influence statistical outcomes, incorporating different independent predictors in the final predictive model for the same ethnic population. However, this assumption has not been evaluated and warrants further study.

Interestingly, among the Taiwanese, the different independent predictors used in the predictive formula of the study sleep laboratory and in Lin et al's[15] formula led to insignificant differences between mean CPAP values, as predicted by the formula from this study and CPAPopt, and between that by Lin et al's[15] formula and CPAPopt. There were similar rates of successful prediction and agreements between the two calculated pressures (CPAPpred1 and CPAPeff) with the observed optimal CPAP (CPAPopt). Thus, in the same ethnic population, one sleep laboratory's own predictive formula for the observed optimal CPAP exhibited the same performance as that of another sleep laboratory, even though different prediction variables were used.

Different ethnic populations have different patient characteristics. Craniofacial abnormalities reportedly have a strong correlation with OSAS in nonobese patients in Asians.[21] When matched by OSAS severity, Asians are significantly less obese than Caucasians.[22,23] However, Asian patients have more severe OSAS than Caucasian patients when matched by obesity.[24,25] In the present study, the mean CPAP values differed significantly only between CPAPopt and those calculated by Miljeteig and Hoffstein's[4] formula, which adopted a different ethnic population as the model-building set. In addition, there were lower rates of successful prediction when applying Miljeteig and Hoffstein's[4] formula in contrast to higher rates of successful prediction when applying the study sleep laboratory's formula or Lin et al's[15] formula, which adopted the same ethnic population as for the model-building set. Despite similar agreements of the three calculated pressures (CPAPpred1, CPAPeff, and CPAPmin) with the observed optimal CPAP (CPAPopt), there was a negatively skewed 95% CI between CPAPopt and CPAP calculated by Miljeteig and Hoffstein's[4] formula. As such, applying a predictive formula derived from a different ethnic population from the study sleep laboratory exhibits performance inferior to that from the same ethnic population used by the study sleep laboratory.

From a literature review, several predictive formulas to calculate the optimal CPAP have been proposed using different ethnic populations (Table 5).[4,6,13–16,24,25] Among

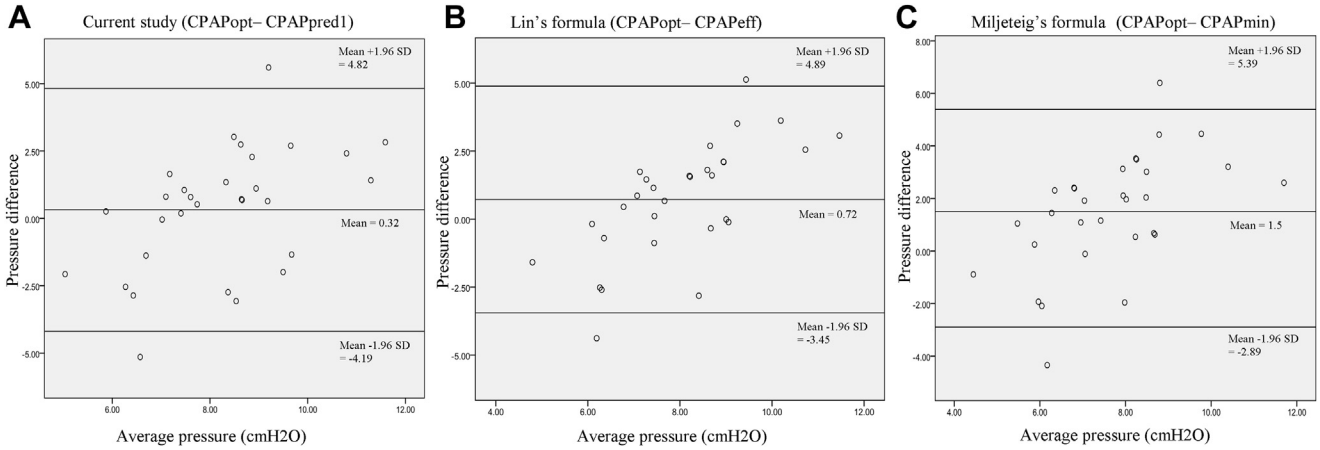

Fig. 3. Agreement between observed optimal CPAP and pressures calculated by three predictive formulas in the validation group. (A) CPAPopt versus CPAPpred1, (B) CPAPopt versus CPAPeff, and (C) CPAPopt versus CPAPmin. Similar agreements of the three calculated pressures were found with the observed optimal CPAP. CPAP = continuous positive airway pressure; CPAPeff = predictive CPAP by Lin et al;[15] CPAPmin = predictive CPAP by Miljeteig and Hoffstein;[4] CPAPopt = observed optimal CPAP; CPAPpred = predictive CPAP by the current study; SD = standard deviation.

them, AHI and BMI are the strongest independent predictors and are selected in most formulas, including the present one in this study. Aside from these two predictors, diverse parameters are selected as prediction variables in different sleep laboratories, parallel with various successful prediction rates or variance. A formula to predict optimal CPAP with both accuracy and simplicity is important for every sleep laboratory, especially in the presence of a long PSG waiting list and contraindications to APAP titration. The present study suggests that a sleep laboratory should build its own predictive formula or adopt one reference formula that is derived from the same ethnic population by another sleep laboratory.

The current study has some limitations. Men with OSAS are more likely to require higher levels of CPAP support than women.[26] Most of the enrolled participants were male, making the accuracy of the study sleep laboratory's predictive formula uncertain in female patients with OSAS. The influence of age on the accuracy of CPAP predictive formulas had also not been reported in previous studies. Only adult patients were enrolled in the present study, making the accuracy of the study sleep laboratory's predictive formula uncertain in pediatric patients with OSAS. Moreover, neither the craniofacial profile nor the history of cardiovascular diseases was recorded in this study. This may have influenced the accuracy of the study sleep

Table 5
CPAP predictive formulas derived from different ethnic populations in different sleep laboratories.

	Study participants for model-building/validation (*n*)	Predictive formula	Successful prediction rate (%)[a]	Variance (%)
Asian population				
Akahoshi et al[14]	170/110	27.78 + (0.041 × BMeH) + (0.141 × BMI) + (0.040 × AHI) - (0.312 × mean SaO_2)	NM	47%
Lin et al[15]	85/36	0.52 + (0.174 × BMI) + (0.042 × AHI)	86%	NM
Chuang et al[16]	418/127	1.98 + (0.184 × BMI) + (0.01 × AHI_{SNS}) + (0.016 × DI_{SNS})	84% in study group, 73% in validation group	NM
Choi et al[24]	202/NM	0.681 + (0.205 × BMI) + (0.040 × AHI)	NM	42%
This study	57/30	6.380 + (0.033 × AHI) − (0.068 × SaO_{2nadir}) + (0.171 × BMI)	56.7%	NM
Caucasian population				
Miljeteig and Hoffstein[4]	38/129	−5.12 + (0.13 × BMI) + (0.16 × NC) + (0.04 × AHI)	NM	76%
Stradling et al[6]	101/NM	(0.048 × ODI) + (0.128 × NC) + 2.1	NM	NM
Schiza et al[13]	991/991 (the same sample population)	For men, 5.16 + (0.003 × smoking in packs/y) + (0.054 × BMI) + (0.016 × AHI) − 0.403 For women, 5.16 + (0.003 × smoking in packs/y) + (0.054 × BMI) + (0.016 × AHI) − 0.806	95%	NM
Loredo et al[25]	76/10% of participants from the original sample	30.8 + (RDI × 0.03) − (SaO_{2nadir} × 0.05) − (mean SaO_2 × 0.2)	NM	67%

AHI = apnea–hypopnea index; BMeH = the angle between a line from point <B> to menton <Me> and a line from Me to the hyoid bone <H>; BMI = body mass index; CPAP = continuous positive airway pressure; DI = desaturation index; NC = neck circumference; NM = not mentioned; ODI = oxygen desaturation index; RDI = respiratory disturbance index; SaO_{2nadir} = nadir of arterial oxyhemoglobin saturation by pulse oximetry; SNS = split-night sleep study.

[a] Successful prediction rate is defined as optimal CPAP being within ±2 cmH_2O of calculated CPAP by predictive formulas.

laboratory's predictive formula in OSAS patients with craniofacial abnormalities or cardiovascular comorbidities. The small sample sizes of the model-building and validation sets may lead to a different set of predictors in the laboratory's predictive formula. However, OSAS patients with mild severity were included in this study to make the study laboratory's predictive formula applicable to cases of mild severity.

In conclusion, a sleep laboratory does not need to construct its own predictive formula for determining the optimal effective CPAP, but should adopt the one derived from the same ethnicity of OSAS patients as used for the reference formula.

References

1. Shiao GM. The rapid development of sleep apnea syndrome. *J Chin Med Assoc* 2009;**72**:283−4.
2. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981;**1**:862−5.
3. Morgenthaler TI, Aurora RN, Brown T, Zak R, Alessi C, Boehlecke B, et al. Standards of Practice Committee of the AASM. 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 update for 2007. An American Academy of sleep medicine report. *Sleep* 2008;**31**:141−7.
4. Miljeteig H, Hoffstein V. Determinants of continuous positive airway pressure level for treatment of obstructive sleep apnea. *Am Rev Respir Dis* 1993;**147**:1526−30.
5. Fitzpatrick MF, Alloway CED, Wakeford TM, MacLean AW, Munt PW, Day AG. Can patients with obstructive sleep apnea titrate their own continuous positive airway pressure? *Am J Respir Crit Care Med* 2003;**167**:716−22.
6. Stradling JR, Hardinge M, Paxton J, Smith DM. Relative accuracy of algorithm-based prescription of nasal CPAP in OSA. *Respir Med* 2004;**98**:152−4.
7. McArdle N, Singh B, Murphy M, Gain KR, Maquire C, Mutch S, et al. Continuous positive airway pressure titration for obstructive sleep apnoea: automatic versus manual titration. *Thorax* 2010;**65**:606−11.
8. 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**:230−4.
9. Hertegonne KB, Volna J, Portier S, De Pauw R, Van Maele G, Pevernagie DA. Titration procedures for nasal CPAP: automatic CPAP or prediction formula? *Sleep Med* 2008;**9**:732−8.
10. Noseda A, André S, Potmans V, Kentos M, de Maertelaer V, Hoffmann G. CPAP with algorithm-based versus titrated pressure: a randomized study. *Sleep Med* 2009;**10**:988−92.
11. Torre-Bouscoulet L, Castorena-Maldonado A, López-Escárcega E, Vázquez-García JC, Pérez-Padilla R. Agreement between 95th percentile pressure based on a 7-night auto-adjusting positive airway pressure trial vs. equation-based predictions in sleep apnea. *J Clin Sleep Med* 2009;**5**:311−6.
12. Marrone O, Salvaggio A, Romano S, Insalaco G. Automatic titration and calculation by predictive equations for the determination of therapeutic continuous positive airway pressure for obstructive sleep apnea. *Chest* 2008;**133**:670−6.
13. Schiza SE, Bouloukaki I, Mermigkis C, Panaqou P, Tzanakis N, Moniaki V, et al. Utility of formulas predicting the optimal nasal continuous positive airway pressure in a Greek population. *Sleep Breath* 2011;**15**:417−23.
14. Akahoshi T, Akashiba T, Kawahara S, Uematsu A, Nagaoka K, Kiyofuji K, et al. Predicting optimal continuous positive airway pressure in Japanese patients with obstructive sleep apnoea syndrome. *Respirology* 2009;**14**:245−50.
15. Lin IF, Chuang ML, Liao MF, Chen NH, Li HY. Prediction effective continuous positive airway pressure in Taiwanese patients with obstructive sleep apnea syndrome. *J Formos Med Assoc* 2003;**102**:215−21.
16. Chuang ML, Lin IF, Vintch JR, Liao YF. Predicting continuous positive airway pressure from a modified split-night protocol in moderate to severe obstructive sleep apnea-hypopnea syndrome. *Intern Med* 2008;**47**:1585−92.
17. Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Bethesda, MD: National Institute of Neurological Diseases and Blindness Neurological Information Network; 1968.
18. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep* 1992;**15**:173−84.
19. Wiest GH, Fuchs FS, Harsch IA, Pour Schahin S, Lampert S, Brueckl WM, et al. Reproducibility of a standardized titration procedure for the initiation of continuous positive airway pressure therapy in patients with obstructive sleep apnoea. *Respiration* 2001;**68**:145−50.
20. Condos R, Norman RG, Krishnasamy I, Peduzzi N, Goldring RM, Rapoport DM. Flow limitation as a non-invasive assessment of residual upper-airway resistance during continuous positive airway pressure therapy of obstructive sleep apnea. *Am J Respir Crit Care Med* 1994;**150**:475−80.
21. Nelson S, Hans M. Contribution of cranio-facial risk factors in increasing apneic activity among obese and non-obese habitual snorers. *Chest* 1997;**111**:154−62.
22. Li KK, Kushida C, Powell NB, Riley RW, Guilleminault C. Obstructive sleep apnea syndrome: a comparison between far-east Asian and white men. *Laryngoscope* 2000;**110**:1689−93.
23. Li KK, Powell NB, Kushida C, Riley RW, Adornato B, Guilleminault C. A comparison of Asian and white patients with obstructive sleep apnea syndrome. *Laryngoscope* 1999;**109**:1937−40.
24. Choi JH, Kim EJ, Kim KW, Choi J, Kwon SY, Lee HM, et al. Optimal continuous positive airway pressure level in Korean patients with obstructive sleep apnea syndrome. *Clin Exp Otorhinolaryngol* 2010;**3**:207−11.
25. Loredo JS, Berry C, Nelesen RA, Dimsdale JE. Prediction of continuous positive airway pressure in obstructive sleep apnea. *Sleep Breath* 2007;**11**:45−51.
26. Jayaraman G, Majid H, Surani S, Kao C, Subramanian S. Influence of gender on continuous positive airway pressure requirements in patients with obstructive sleep apnea syndrome. *Sleep Breath* 2011;**15**:781−4.