Obstructive Sleep Apnea: A Canonical Correlation of Cephalometric and Selected Demographic Variables in Obese and Nonobese Patients

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Abstract: One hundred male obstructive sleep apnea (OSA) patients were classified into 2 groups on the basis of body mass index (BMI): 43 nonobese (BMI < 30 kg/m²) and 57 obese (BMI \ge 30 kg/m²) patients. A comprehensive cephalometric analysis with a multivariate statistical method was performed in order to define the different principal components (PCs) of cervico-craniofacial skeletal and upper airway soft tissue morphology in each group and how they contributed to selected elements of the patient demographic data, ie, apnea-hypopnea index (AHI), nocturnal oxyhemoglobin saturation, and BMI. Thirty cephalometric variables of cervico-craniofacial skeletal morphology were reduced to 8 PCs describing 84.4% and 85.4% of the total variance in obese and nonobese OSA patients, respectively. Sixteen cephalometric variables of hyoid bone position and head posture were reduced to 4 PCs describing 84.4% and 85.9% of the total variance in obese and nonobese OSA patients, respectively. Twenty cephalometric variables of upper airway soft tissue morphology were reduced to 7 PCs describing 89.5% and 84.6% of the total variance in obese and nonobese OSA patients, respectively. For further analysis of PCs, a stepwise multiple regression analysis was chosen. Two dependent variables of interest are the minimal distance of the posterior pharyngeal airway space (PASmin) and AHI. PASmin accounted for 95.3% (obese OSA group) and 74.3% (nonobese OSA group) with 7 PCs and AHI for 46% with 3 PCs in both groups. Three canonical variables and their correspondents with different loadings were established differently for both OSA groups. A canonical correlation successfully clarified the complexity of simultaneous relationship of the relevant variables. These analyses are proved useful to demonstrate the relationship of cervico-craniofacial skeletal and upper airway soft tissue morphology and selected demographic data. This lays down a basis for understanding the complicated pathogenic components of obese and nonobese OSA patients. (Angle Orthod 2001;71:23–35.)

Key Words: Obstructive sleep apnea; Obesity; Cephalometric analysis; Multivariate analyses

INTRODUCTION

Recently, a survey of health care utilization among 181 obstructive sleep apnea (OSA) patients showed that during

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the 10 years before diagnosis they had already been heavy users of health services for several years.¹ The estimated cost of this care was twice as much as that of average patients. This finding reflected the underlying risk factors such as obesity² and alcohol³ and tobacco consumption⁴ in OSA patients. Aside from the predisposing factors, the deleterious consequences of OSA were mainly caused by sleep fragmentation,⁵ hypoxemia, and increased systemic or pulmonary hypertension.⁶ Sleep fragmentation leads to excessive daytime sleepiness, related harmful effects in cognitive functions, and increased risks of automobile accidents.⁷

Despite its being a life-threatening disease, the pathogenesis of OSA remains obscure.⁸ Recurrent cessation of breathing with simultaneous respiratory attempts during night sleep is the main feature of OSA. The nocturnal respiratory tract occlusion occurs at the upper airway level.⁹ Upper airway patency is determined by an interactive role of anatomic and neuromuscular factors. Craniofacial skel-

	Nonobese O (n =	SA Patients 43)	Obese OSA Patients $(n = 57)$		Obese OSA Patients $(n = 57)$			
Variable	Mean \pm SD	Range	Mean \pm SD	Range	F Values			
Age, y	48.3 ± 11.8	20.9-70.0	48.5 ± 11.7	25.2-68.4	0.0			
Height, cm	178.5 ± 6.6	164.0-194.0	178.7 ± 6.2	169.0-194.0	0.0			
Weight, kg	84.5 ± 10.6	62.0-112.0	109.5 ± 12.1	89.0-139.0	105.3*			
BMI, kg/m ²	26.5 ± 2.7	19.4-29.0	34.3 ± 3.6	30.1-43.3	138.5*			
AHI, events per hour	32.2 ± 17.7	11.0-70.0	48.4 ± 28.8	11.0–115.0	9.5*			
SaO ₂ , %	76.2 ± 9.4	49.0-93.0	70.0 ± 13.5	45.0-89.0	16.6*			

TABLE 1. Demographic Data for OSA Patients^a

^a BMI indicates body mass index; AHI, apnea-hypopnea index; SaO₂, oxyhemoglobin saturation; and OSA, obstructive sleep apnea. * *P* < .001

etal and upper airway soft tissue morphology, obesity, sleep position, and nocturnal genioglossus activity represent a few examples of the determinants.10 The diagnosis of OSA can be confirmed only by overnight polysomnography.¹¹ Among the many outcome parameters, the apnea-hypopnea index (AHI) and the minimal oxyhemoglobin saturation are variables of interest. OSA severity is usually expressed in terms of AHI. The AHI, indicating the number of respiratory irregularities per sleep hour, is calculated with this formula: [(total number of apneas + hypopneas)/(total sleep time in minutes)] \times 60. An index value exceeding 5 indicates the presence of OSA.12 Upper airway obstruction can be confirmed by respiratory effort registration recorded by thoracic-abdominal strain gauge and electromyogram measurements.13 Prolonged nocturnal oxyhemoglobin desaturation in OSA patients may be responsible for symptoms such as cognitive impairment, delirium, morning headache, and daytime hypersomnolence.14 Obesity can be associated with mild to severe respiratory functional impairment.15 Increasing obesity is associated with decreasing oxyhemoglobin saturation, resulting in 2 primary disorders: obesityhyperventilation syndrome¹⁶ and sleep apnea.¹⁷

Lateral cephalometric radiography has proved to be a very useful tool to assess the cervico-craniofacial skeletal and upper airway soft tissue morphology in OSA patients.^{18–24} OSA patients have been shown to have a narrow antero-posterior cranial base and bony pharynx, retrognathic maxilla and mandible, inferiorly positioned hyoid bone, deviated head posture, enlarged soft palate and tongue, and strait airway space.^{21,22}

Nevertheless, the simultaneous relationship between cephalometric variables describing cervico-craniofacial morphology and demographic data such as OSA severity, minimal oxyhemoglobin saturation, and body mass index (BMI) has never before been described. In addition, the prediction power of cervico-craniofacial morphology with respect to OSA severity in OSA subgroups was previously reported in only very few studies and with a wide range of results (26% to 69%).^{25,26} The purpose of this paper was to define the simultaneous relationships between OSA severity, BMI, lowest oxyhemoglobin saturation, and cervico-

craniofacial skeletal and upper airway soft tissue morphology in each group.

MATERIALS AND METHODS

One hundred dentate white men with OSA were included in the study. The ages ranged from 21 to 70 years (mean 52.5 years). All patients had a history of disturbed sleep characterized by heavy snoring and recurrent apneic periods, as well as excessive daytime sleepiness. They underwent a physical evaluation, including head and neck and neurological examination, pulmonary and cardiac function tests, and 24-hour Holter electrocardiogram.²⁷ All-night polysomnographic recordings documented the presence of OSA in all patients. The sleep recording included electroencephalogram, electrocardiogram, electrooculogram, electromyogram, thoracic respiratory movements, oro-nasal airflow, and oxyhemoglobin saturation with pulse oximetry.²⁸ The cutoff point of BMI $> 30 \text{ kg/m}^2$ was used to divide OSA patients into 2 groups of obesity and nonobesity. The demographic data of the OSA patients are summarized in Table 1.

Cephalometric analysis

All the lateral cephalograms were taken with a Lumex B (Siemens Norge A/S; Oslo, Norway) cephalostat with an intensifying screen and a motorized adjustable grid. The peak kilovoltage was adjusted to optimize the contrast of both hard and soft tissues. The distance from the focus to the median plane was 180 cm, and the distance from the median plane to the film was 10 cm. The subject was seated with the median plane parallel to the film, with maximal intercuspation of the teeth, with the lips in light contact, and in a natural head position.²⁹ A possible lateral head tilt or rotation was prevented by means of a cross light beam projected onto the face, and finally, bilateral ear rods were gently inserted into the external part of the auditory canal to stabilize the head posture during exposure. The enlargement was 5.6%; this was not corrected. All lateral cephalograms were taken before any medical or surgical intervention. The reference points and lines used in the cepha-



FIGURE 1. Cervico-craniofacial skeletal reference points used in this study: aa, anterior atlas; ar, articulare; ba, basion; c2, c3, c4, cervical vertebrae 2, 3, and 4; gn, gnathion; go, gonion; n, nasion; or, orbitale; p, palate; pg, pogonion; pgn, prognathion; pm, pterygomaxillare; po, porion; s, sella; sm, supramentale; sp, spinale; ss, subspinale; AH, anterior hyoid. (Reproduced with kind permission of the editors of the *Journal of Laryngology and Otology.*)³¹



FIGURE 3. Reference points and lines used to study head posture: NSL, nasion-sella line; FH, Frankfort horizontal line; NL, nasal line; OPT, odontoid process tangent; CVT, cervical vertebra tangent; VER, true vertical; HOR, true horizontal.³³ (Reproduced with kind permission of Oxford University Press.)³¹

lometric analysis are given in Figures 1 through 5. The definitions have been described in previous papers.^{30–33}

Reliability

All the lateral cephalograms were traced twice by hand on acetate tracing paper and digitized twice to the Dento-



FIGURE 2. Reference lines used in this study: FH, Frankfort horizontal line; ML, mandibular line; NL, nasal line; NP, nasion perpendicular; OL, occlusal line; NSL, nasion-sella line; RL, ramus line; AH-C3 Hor, horizontal position of hyoid bone related to the third cervical vertebra; AH-C3 Ver, vertical position of hyoid bone related to the third cervical vertebra. (Reproduced with kind permission of the editors of the *Journal of Laryngology and Otology*.)³¹



FIGURE 4. Uvulo-glossopharyngeal reference points used in this study: AH, anterior hyoid; GE, genial tubercle; H, highest dorsal point of the tongue; LPW, lower pharyngeal wall; MPW, middle pharyngeal wall; T, tip of the tongue; U, tip of the uvula; UPW, upper pharyngeal wall; V, vallecula. (Reproduced with kind permission of the editors of the *Journal of Laryngology and Otology*.)³²

facial Planner computer program (Dentofacial Software Inc, Toronto, Canada) on an IBM 286/AT desktop computer. The second episode of tracing and digitizing was done 2 weeks apart from the first one. If the difference exceeded 1 mm or 1°, a third measurement was taken, and the middle value of the 2 closest measurements was used. By using Dahlberg's³⁴ formula,

$$\left(S_e = \sqrt{\frac{\sum d^2}{2n}}\right),$$

the measurement error for a single measurement of linear and angular variables ranged between 0.15 and 0.88 mm/ degrees. Houston's coefficient of reliability³⁵ ranged from 82% to 98%. No systematic errors were detected. All area measurements were made in the same manner on an Apple Europlus II computer (Apple Computer, A/S Skøyen, Norway) that gave mean values and standard deviations. All precautions were taken to minimize the errors of the study and the measurement.^{36–38}

Statistics

In order to analyze the relationships among OSA severity, BMI, the minimal oxyhemoglobin saturation, and cephalometric variables, a canonical correlation analysis was performed. A prior procedure included the reduction of numerous cephalometric variables to a few and meaningful principal components (PCs) by using a principal component analysis (PCA).

Principal component analysis

PCA³⁹ is a multivariate statistical model that expedites the reduction of the number of variables. The set of variables should have some correlation. Two required basic assumptions, ie, the Kaiser-Meyer-Olkin measurement of sampling adequacy and Bartlett's test of sphericity, must be verified. The approved range of values of Kaiser-Meyer-Olkin (0.7 to 1.0) indicates the sample size sufficiency. The significance level of Bartlett's test of sphericity demonstrates the equal variance among the group of variables. A small set of new variables, which are linear combinations of the original variables, can be identified with most of the original information contained therein. The first PC is a linear combination of the original variables, which accounts for the largest possible proportion of the variance. The second component is a linear combination of the original variables, which explains the second largest proportion of the variance, subject to the constraint that it is orthogonal to the first component, and so on. The detail and procedure of PCA was previously described.40

Canonical correlation analysis

Canonical correlation analysis⁴¹ is a multivariate statistical model that facilitates the study of interrelationships



FIGURE 5. Area measurements used in this study. (A) Tongue area (TA): the outline starts from V (vallecula) through H (highest dorsal point of the tongue) to T (tip of the tongue) and the lines to GE (genial tubercle), AH (anterior hyoid), and back to V. (B) Soft palate area (SPA): the outline includes the anterior and posterior contour of the soft palate. The superior border was a line through pterygomaxillare (pm) perpendicular to the pm-U line. (C) Residual oral area: included with TA to form oral area (OA). (D) Pharyngeal area (OPA).

among sets of multiple dependent and independent variables. Canonical correlation analysis identifies the optimal structure or dimensionality of each variable set that maximizes the relationship between composites of sets of multiple dependent and independent variables. In doing so, it develops a number of independent canonical functions that maximize the correlation between the linear composites, also known as canonical variates, which are sets of dependent and independent variables. Each canonical function is actually based on the correlation between 2 canonical variates, 1 variate for the dependent variables and 1 for the independent variables. Another unique feature of canonical correlation is that the variates are derived to maximize their correlation. Moreover, canonical correlation does not stop with the derivation of a single relationship between the sets of variables. Instead, a number of canonical functions (pairs of canonical variates) may be derived.

If the 2 groups of variables $[X_1, X_2, ..., X_s]$ and $[Y_1, Y_2, ..., Y_t]$ are observed for *n* cases, canonical variates could be formed by using the least squares method to calculate the coefficients of each variable in both groups. The *k*th pair of canonical variates would be

No.	Principal Components	Eigenvalues	Cumulative % Variance
	(Obese n = 57)		
1 1	AEH + (ar - pgp) + ALEH + ALIEH + (ML/NSL)	4 669	15 565
12	$(ss \mid NP) + (pg \mid NP) + snpg + snsg + snsg$	3 722	27 971
1.3	$(pq \perp NP) + sppq + spsm + OVFRBITE + spsm$	3.419	39.367
1.4	(pm - aa) + (n - ba) + (s - ba) + (pm - ba)	3.390	50.665
1.5	PLFH + PFH + (ML/NSL) + (PU/PLFH)	3.268	61.560
1.6	(NL/NSL) + (FH/NSL) + snba	3.052	71.734
1.7	(s - n) + (sp - pm)	2.008	78.426
1.8	$(ML/RL) + (p \perp OL)$	1.751	84.447
	(Nonobese n = 43)		
1.1	$(ss \perp NP) + (pg \perp NP) + snpg + snsm + snss$	5.971	19.903
1.2	$ALFH + AFH + (p \perp OL) + (ML/NSL) + (ML/RL) + (ar - pgn)$	4.475	34.821
1.3	AUFH + (NL/NSL) + (FH/NSL) + snba + (AU/ALFH)	4.201	48.824
1.4	(s - ba) + (n - ba) + (pm - aa) + (pm - ba)	2.948	58.651
1.5	PFH + PLFH + (ML/RL) + (PU/PLFH) + (ML/NSL)	2.197	65.973
1.6	$ssnsm + OVERJET + (pg \perp NP) + snpg + snsm$	2.178	73.234
1.7	(sp - pm) + (go - gn) + (s - n)	1.834	79.346
1.8	PUFH + (PU/PLFH) + (NL/NSL)	1.814	85.394

TABLE 2. PCA Results of Craniofacial Skeletal Morphology in Obese and Nonobese OSA Patients^a

^a PCA indicates principal component analysis; OSA, obstructive sleep apnea.

$$P_k = u_1 X_1 + u_2 X_2 + \dots + u_s X_s$$

 $Q_k = v_1 Y_1 + v_2 Y_2 + \dots + v_t Y_t$

Coefficients of canonical variables (u,v) are called *eigen*vectors. Correlation between P_k and Q_k are termed *canonical correlations* (R_k). Eigenvectors are chosen so that the canonical correlation is as high as possible, subject to the constraint that (P_k , Q_k) are uncorrelated with [P_1 , Q_1 ; P_2 , Q_2 ; ..., P_{k-1} , Q_{k-1}]. Apparently, $R_1 > R_2 > ... R_{(s,t)}$. If there is a great deal of interdependency between the 2 groups of variables, several canonical variables may be needed to express this relationship. The significance of the canonical correlations can be tested by means of Bartlett's chi-square test. Canonical variables can be interpreted by evaluating the canonical variables (X_s , Y_t) with canonical variables (P_k , Q_k). All statistical analyses were performed with SPSS for Windows 8.0.2 (SPSS Inc, Chicago, III).

RESULTS

Reduction of the original variables

The prerequisite of the PCA includes Bartlett's test of sphericity (P < .000) and the measurement of sampling adequacy with the Kaiser-Meyer-Olkin method (KMO \ge 0.700). Our results were within the acceptable range. Varimax rotation was used for sensible interpretations. PCs were chosen if the eigenvalues were ≥ 1 .

Craniofacial skeletal morphology

Eight PCs (linear combinations which accounted for approximately 85% of the total variance) that were obtained

for the 30 original variables in both groups of obese and nonobese OSA patients are presented in Table 2. The factor loadings give the strength and direction of the variables that contribute to the PCs. Without comparing with the controls, PCA was able to demonstrate the disconfiguration of the craniofacial skeleton (Figures 1 and 2) in both groups. The leading feature in the obese OSA group was due to the increased anterior facial height (AFH; anterior upper facial height (AUFH), anterior lower facial height (ALFH)), mandibular length, and mandibular plane angle, which was represented as PC 1.1 (eigenvalue = 4.669; 15.565% of total variance). In the nonobese OSA patient group, the combination of narrow antero-posterior dimension of maxilla and mandible and retruded chin was the first PC (eigenvalue = 5.971; 19.903% of total variance). Comparison between the obese and nonobese OSA patients showed that the 8 PCs differed in sequence, direction, and magnitude. PCs used in the subsequent canonical correlation analysis are listed in Table 2.

Head posture and hyoid bone position

Four PCs were procured for the 17 original variables in both OSA groups (Table 3). The magnitude and direction of cephalometric variables contributed to the principal components expressed as factor loadings. The components of PCs were almost the same in both OSA groups, except that the sequence and values were different. PCs 2.1 and 2.2 (> 55% of variance) exhibited the divergence of head posture (Figures 2 and 3), whereas PCs 2.3 and 2.4 gave the deviant amount of hyoid bone position. Explicitly, the hyoid bone was located inferiorly in both OSA groups. The hyoid bone

No.	Principal Components	Eigenvalues	Cumulative % Variance
	(Obese n = 57)		
2.1	(NSL/OPT) + (FH/CVT) + (FH/OPT) + (NL/OPT) + (NSL/CVT) + (NL/CVT) + (CVT/HOR) + (OPT/HOR)	6.695	39.382
2.2	(NL/VER) + (NSL/VER) + (FH/VER)	3.166	58.005
2.3	$(AH \perp FH) + (AH - s Ver) + (AH \perp C3) + (AH \perp ML)$	3.162	76.604
2.4	(AH - C3) + (OPT/CVT)	1.334	84.450
	(Nonobese n = 43)		
2.1	(FH/CVT) + (FH/OPT) + (NSL/CVT) + (NL/CVT) + (NL/OPT) + (NSL/OPT) + (OPT/HOR) + (CVT/HOR)	6.137	36.099
2.2	(NSL/VER) + (NL/VER) + (FH/VER)	3.283	55.411
2.3	$(AH \perp FH) + (AH - s Ver) + (AH \perp ML) + (AH \perp C3)$	3.118	73.755
2.4	(AH - C3) + (OPT/CVT)	2.064	85.898

TABLE 3. PCA Results of Head Posture and Hyoid Bone Position in Obese and Nonobese OSA Patients^a

^a PCA indicates principal component analysis; OSA, obstructive sleep apnea.

TABLE 4. PCA	Results of Upper	Airway Soft Tis	ue Morphology ir	n Obese and	d Nonobese	OSA P	atients
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No.	Principal Components	Eigenvalues	Cumulative % Variance
	(Obese n = 57)		
3.1	TA + OA + OPA + (V - T)	4.018	20.091
3.2	SPA + SPA/(OPA - OA) + SPT + (NL/pm - U)	3.411	37.145
3.3	(pm - UPW) + (U - MPW) + PASmin	2.907	51.680
3.4	$(TA/OA) + (TA + SPA)/(OPA + (H \perp VT))$	2.199	62.675
3.5	$(VT/FH) + (V \perp FH)$	2.085	73.102
3.6	(V - C3) + (V - LPW)	1.993	83.066
3.7	(pm - U) + CL	1.740	89.594
	(Nonobese n = 43)		
3.1	PASmin + pm - UPW + (NL/pm - U) + (U - MPW)	3.796	18.979
3.2	SPA + SPA/(OPA - OA) + SPT	2.594	31.951
3.3	OPA + OA + TA + (V - T)	2.399	43.945
3.4	(V - C3) + (V - LPW)	2.274	55.313
3.5	$(VT/FH) + (V \perp FH)$	2.122	65.922
3.6	$(TA + SPA)/OPA + (TA/OA) + (H \perp VT)$	2.003	75.936
3.7	(pm - U) + CL	1.740	84.635

^a PCA indicates principal component analysis; OSA, obstructive sleep apnea.

assumed an anterior position away from cervical column only in obese OSA patients.

Upper airway soft tissue

Seven PCs represented 20 original cephalometric variables (Table 4). Linear combination of increased size of tongue, oral area (OA), and oropharyngeal area (OPA) represented the first PC of obese OSA patients (eigenvalues = 4.018). In the nonobese group, narrow minimal posterior pharyngeal airway space (PASmin), nasopharynx, velopharynx, and decreased angulation between uvula and palatal plane (NL/pm-U) set forth the first PC (eigenvalue = 3.796). This expressed the different leading elements of upper airway soft tissue between the obese and nonobese groups (Figures 4 and 5).

Further analysis of principal components

Stepwise multiple regression. Two dependent variables of interest, AHI and PASmin, were chosen for a stepwise multiple regression with all PCs as independent variables.

The PASmin variable (Tables 5 and 6) was removed from PC 3.2 of the obese OSA and from PC 3.1 of the nonobese OSA patients before the multiple regression process. The appropriateness of the multiple regression analysis was indicated by a Durbin-Watson value that was close to the value of 2 in both groups. The correlation coefficient (R; 0.976, 0.862) revealed a strong relationship between PASmin and the selected PCs in both groups of OSA patients. The coefficient of determination (R²; 0.953, 0.743) indicated that PCs could explain up to 95.3% and 79.4% of PASmin in obese and nonobese OSA patients, respectively. The

 TABLE 5.
 Summary of Stepwise Multiple Regression Between PASmin and All PCs in Obese OSA Patients^a

R	R ²	Adjust R ²	Durbin-Watson
0.976	0.953	0.885	2.025
		ANOVA	
	Sum of Square	F-value	Significance
Regression	577.906	14.024	.000
	(Coefficients	
PC –	В	Beta	Significance
PC	B 10.255	Beta	Significance
PC Constant PC 3.1	B 10.255 4.085	Beta 	Significance .000 .000
PC Constant PC 3.1 PC 3.2	B 10.255 4.085 3.820	Beta — 0.939 0.783	Significance .000 .000 .000
PC Constant PC 3.1 PC 3.2 PC 3.5	B 10.255 4.085 3.820 2.182	Beta 0.939 0.783 0.517	Significance .000 .000 .000 .000
PC Constant PC 3.1 PC 3.2 PC 3.5 PC 3.6	B 10.255 4.085 3.820 2.182 2.120	Beta 0.939 0.783 0.517 0.487	Significance .000 .000 .000 .000 .000
PC Constant PC 3.1 PC 3.2 PC 3.5 PC 3.6 PC 1.5	B 10.255 4.085 3.820 2.182 2.120 -1.227	Beta 0.939 0.783 0.517 0.487 -0.282	Significance .000 .000 .000 .000 .001 .003
PC Constant PC 3.1 PC 3.2 PC 3.5 PC 3.6 PC 1.5 PC 2.3	B 10.255 4.085 3.820 2.182 2.120 -1.227 -1.365	Beta 0.939 0.783 0.517 0.487 -0.282 -0.314	Significance .000 .000 .000 .000 .001 .003 .005

 $^{\rm a}$ PASmin indicates minimal distance of the posterior pharyngeal airway space; PC, principal component; and OSA, obstructive sleep apnea, n = 57.

TABLE 6. Summary of Stepwise Multiple Regression Between PASmin and all PCs in Nonobese OSA Patients^a

R	R ²	Adjust R ²	Durbin-Watson
0.862	0.743	0.621	2.159
		ANOVA	
	Sum of Square	F-value	Significance
Regression	352.282	6.096	.000
_	(Coefficients	
PC	В	Beta	Significance
Constant	8.016	_	.000
PC 1.1	0.830	0.285	.001
PC 1.4	0.691	0.233	.004
PC 3.1	0.587	0.201	.006
PC 3.2	-0.963	-0.331	.009
PC 3.3	-0.725	-0.249	.002
PC 3.6	-0.546	-0.177	.001
PC 2.2	-1.262	-0.434	.000

 $^{\rm a}$ PASmin indicates minimal distance of the posterior pharyngeal airway space; PC, principal component; and OSA, obstructive sleep apnea, n = 43.

significance of analysis of variance confirmed the linear relationship between them. The standardized coefficients (beta) yielded the robustness of each PC. The PCs that related to PASmin were different in each OSA group. In the obese OSA group, the first PC (PC 3.1) was a combination of increased tongue area, OA, OPA, and tongue length. The second PC (PC 3.2) was a combination of the increased size and length of uvula (SPA, SPA/(OPA-OA), SPT) and its decreased angulation to the palatal plane (NL/pm-U). These PCs were prior elements that determined the size of PASmin. On the other hand, skeletal components such as
 TABLE 7. Summary of Stepwise Multiple Regression Between AHI

 and All PCs in Obese OSA Patients^a

R	R R ²		Durbin-Watson
0.672	0.452	0.414	1.958
		ANOVA	
	Sum of Square	F-value	Significance
Regression	13308.184	13308.184 3.957	
	C	Coefficients	
PC B		Beta	Significance
Constant 49.097		_	.000
PC 3.1	28.927	0.932	.000
PC 2.3	13.275	0.584	.000
PC 3.2	-19.696	-0.791	.000

 a AHI indicates apnea-hypopnea index; PC, principal component; and OSA, obstructive sleep apnea, n = 57.

 TABLE 8. Summary of Stepwise Multiple Regression Between AHI

 and All PCs in Nonobese OSA Patients^a

R	R ²	Adjust R ²	Durbin-Watson	
0.679	0.460	0.119	2.077	
		ANOVA		
	Sum of Square	F-value	Significance	
Regression	7046.328	3.875	.007	
	(Coefficients		
PC	В	Beta	Significance	
Constant	31.394	_	.000	
PC 1.1	12.622	0.711	.001	
PC 3.1	-9.696	-0.491	.002	
PC 2.4	8.175	0.484	.005	

 $^{\rm a}$ AHI indicates apnea-hypopnea index; PC, principal component; and OSA, obstructive sleep apnea, $n\,=\,43.$

maxillomandibular retrognathism and retruded chin (PC 1.1: $ss \perp NP$, $pg \perp NP$, snpg, snsm, snss), narrow cranial base, nasopharynx and velopharynx (PC 1.4: s-ba, n-ba, pm-aa, pm-ba) rendered the PASmin dimension in the nonobese OSA group.

The AHI is shown in Tables 7 and 8. In both OSA groups, the appropriateness of the multiple regression analysis was verified by the Durbin-Watson value (1.958, 2.077). R (0.672, 0.679) revealed the strength of relationship between AHI and the selected PCs. R^2 (0.452, 0.460) exhibited that PCs could explain up to 45.2% and 46% of AHI in obese OSA and nonobese OSA patients, respectively. The significance of analysis of variance confirmed the linear relationship between them. The standardized coefficients (beta) yielded the robustness of each PC. The PCs that significantly related to AHI in obese OSA patients included increased size and length of tongue, OA, and OPA; inferiorly located position of the hyoid bone; and increased

			Bartlett's Test for Remaining Eigenvalues				
Eigenvalue Canonical Correlation Eige		Eigenvalue	Wilk's Lambda	Chi-square	Degree of Freedom	Significance	
Obese							
1	0.980	0.960	0.000	109.103	57	.000	
2	0.967	0.935	0.009	77.122	36	.001	
3	0.926	0.857	0.013	50.393	27	.010	
Nonobese							
1	0.874	0.764	0.069	83.032	57	.007	
2	0.746	0.557	0.092	51.232	36	.010	
3	0.722	0.521	0.356	32.749	27	.033	

TABLE 9. Results of Canonical Correlation Between Demographic Data and Principal Components of Cephalometric Variables of Obese^a and Nonobese^b OSA Patients^a

^a OSA indicates obstructive sleep apnea.

size and length of the soft palate and its decreased angulation to the palatal plane.

The PCs that significantly related to AHI in nonobese OSA patients included maxillomandibular retrognathism and retruded chin; decreased PASmin, nasopharynx and velopharynx, and a decreased angulation of uvula to palatal plane; and decreased cervical lordosis.

Canonical correlation analysis. Canonical correlations (Table 9) determined the holistic relationship among the selected demographic variables and the PCs. Bartlett's test indicates the number of canonical variables necessary to express the dependency between the 2 sets of variables, that is, the smallest number of eigenvalues so that the test of the remaining eigenvalues is nonsignificant. In the present study, the .05 level of significance was tested. Three canonical correlations (obese OSA group, r1 = 0.980, P =.000; r2 = 0.967, P = .001; r3 = 0.967, P = .010; nonobese OSA group, r1 = 0.874, P = .007; r2 = 0.746, P $= .010; r_3 = 0.722, P = .033$) were found to be highly significant in both OSA groups. Canonical variable loadings for the demographic and PCs variables gave robustness and trend. Since 21 canonical variable loadings were considered concurrently for each set of canonical variables, it was determined that the correlation coefficient could be declared significant at an overall 5% level if its absolute value was larger than 0.399. Therefore, the decision to neglect canonical variable loadings smaller than 0.400 was adopted. The absolute values of the canonical variable loadings were interpreted as light ($0.4 \le r \le 0.5$), moderate ($0.5 \le r \le$ 0.7), and heavy $(0.7 \le r \le 1.0)$.

The obese OSA group is shown in Figure 6. The first canonical variable for the demographic variable group had a heavy negative loading with oxyhemoglobin saturation. The corresponding first canonical PCs variable group showed heavy positive loadings with PCs 2.1, 2.2, and 2.3, 2 moderate positive loading with PCs 1.2 and 3.1, and a light positive loading with PC 3.6. Only one moderate negative loading was determined in PC 2.4. The eigenvalue for the first canonical correlation indicated that approximately

96% of the variation in the first canonical demographic variable could be accounted for by the interdependence with the first canonical PCs variable. The second canonical variable for the demographic variable group revealed a heavy positive loading for BMI. The concomitant second canonical variable for the PCs variable group had heavy positive loadings for PCs 3.1, 3.2, and 3.7 and light positive loadings for the proportion of tongue and soft palate to OA and OPA and tongue height and its position were identified (PCs 3.4 and 3.5). The eigenvalue for the second canonical correlation indicated that nearly 94% of the variation in the second canonical demographic variable could be explained by an association with the second canonical PCs variable. By definition, the association determined by the second canonical correlation was statistically independent from that of the first.

The third canonical variable for the demographic variable group had a heavy positive loading with AHI. The corresponding canonical variable for the PCs variable group showed 4 almost equal heavy positive loadings with PCs 3.1, 3.2, 3.3, and 3.7, 1 moderate positive loading with PCs 1.1 and 2.1, and 2 light positive loadings with PCs 3.4 and 3.5. The third canonical correlation was statistically independent from the first and second correlations, and approximately 86% of the variation in the third canonical demographic variable could be explained by a relationship with the concomitant PCs variable.

The nonobese OSA group is shown in Figure 7. The first canonical variable for the demographic variable group had a moderate negative loading with BMI and a heavy negative loading with oxyhemoglobin saturation. The cognate first canonical PCs variable group showed a moderate positive loading with PC 1.7 and 4 moderate negative loadings with PCs 1.1, 1.6, 2.1, and 2.2. The eigenvalue for the first canonical correlation indicated that approximately 76% of the variation in the first canonical demographic variable could be accounted for by the interdependence with the first canonical PCs variable. The second canonical variable for the demographic variable group revealed a heavy positive





FIGURE 6. Graphic presentation of canonical correlation between demographic and principal components group in obese patients with obstructive sleep apnea.

loading solely for AHI. The concomitant second canonical variable for the PCs variable group had heavy positive loadings for PCs 1.1, 1.2, and 1.7; moderate loadings for PCs 1.4 and 2.3, and 2 light positive loadings for PCs 3.1 and 3.2. The eigenvalue for the second canonical correlation indicated that nearly 56% of the variation in the second canonical demographic variable could be explained by an

association with the second canonical PCs variable. By definition, the association determined by the second canonical correlation was statistically independent from that of the first.

The third canonical variable for the demographic variable group had a heavy negative loading with oxyhemoglobin saturation and a moderate negative loading with BMI. The



FIGURE 7. Graphic presentation of canonical correlation between demographic and principal components group in nonobese patients with obstructive sleep apnea.

corresponding canonical variable for the PCs variable group showed 2 heavy positive loadings with PCs 2.1 and 2.2; 3 moderate positive loadings with PCs 1.1, 1.2, and 1.5; and 2 light positive loadings with PCs 3.1 and 3.2. The third canonical correlation was statistically independent from the first and second correlations, and approximately 52% of the variation in the third canonical demographic variable could be explained by a relationship with the concomitant PCs variable.

DISCUSSION

The cause of obstructive sleep apnea is very complex and not yet fully understood. The interaction between deviated anatomical features and aberrated physiological factors plays an important role for the OSA etiology. Lateral cephalometry is a very useful simple tool to assess the morphology of the upper airway and its related structures. In modern morphometrics, the use of the multivariate statistical method is necessary to interpret the complexity of interdependent variables.⁴² In this study, PCA (which is a subset of factor analysis), stepwise multiple regression, and canonical correlation analysis were used. Factor analytic statistical methods have been used extensively to extract the latent components that account for observable craniofacial morphology and to summarize its overall characteristics.^{30,40,43} PCA was used simply to reduce a number of cephalometric variables to a smaller set of composite variables with a minimum loss of information. A combination of the original variables was designed so that the PCs could be easily interpreted from a biologic viewpoint. The existence of different morphologic features in OSA subgroups was reported by several studies.^{25,44,45} By PCA, our study showed that both obese and nonobese OSA patients had atypical cervico-craniofacial skeletal as well as upper airway soft tissue morphology. Nevertheless, the fundamental characteristics were different from each other. For instance, PC 1.1 in each group did not have the same elements. The authentic dissimilarity between groups could be clearly seen when related to the dependent variables such as AHI and PASmin. In the obese OSA group, the severity was primarily related to the aberrant tongue and soft palate and the inferior position of the hyoid bone. On the other hand, the maxillomandibular retrognathism, retruded chin, narrow pharyngeal airway space, and decreased cervical lordosis were precedingly affiliated with AHI in the nonobese group. The PCs could explain up to 45–46% of the variance in AHI. This was higher than previous studies that have reported prediction values of 26%,⁴⁶ 32%,²⁶ 33%,²⁵ and 42%.45 Only Mayer et al25 found that upper airway variables in young or lean patients could explain higher variance in AHI (55% and 69%, respectively). The wide range of prediction power is mainly due to the selection of the different kind of upper airway variables. The advantage of using PCs is the ability to include meaningful and comprehensive variables that could be all taken into account at the same time without losing necessary information.

The emergence of the minimal distance of the posterior PASmin measurement, which could be one of the most likely obstruction sites in our previous studies,^{21,22,31,32} was supported by the measurement method of Solow et al.47 PASmin resembled the perpendicular distance from radix linguae to the nearest point on the dorsal pharyngeal wall in their study. This is quite different from the pharyngeal airway space previously proposed by Riley et al.¹⁸ The pharyngeal airway space measured along the B-Go lines and represented a more or less oblique diameter of the pharyngeal airway, usually located at the base of the tongue. This could give a wide range of uncertainty. Interestingly, PCs in the obese OSA group could explain more of the variance (95.3%) of PASmin than that of the nonobese group (74.3%). This could be interpreted that PASmin was better accounted for by upper airway soft tissue morphology among the obese OSA patients.

Canonical correlation analysis has been applied to morphometric studies^{48,49} in an attempt to solve the complexity of the interrelationships between craniofacial structures and their related functions. In obese OSA patients, the interpretation of the first canonical correlation was that the decreased oxyhemoglobin saturation was closely related to upward, forward, and extended head posture (PCs 2.1 [+0.820], 2.2 [+0.781], and 2.4 [-0.640]; lower position of hyoid bone (PC 2.3 [+0.811]); increased tongue size and its forwarded vallecula position (PCs 3.1 [+0.533], 3.6 [+0.421]); maxillomandibular retrognathism; and retruded chin (PC 1.2 [+0.421]). In the nonobese group, there were 2 categories of patients. The first group, resulting from the first canonical correlation, was nonobese OSA patients without a serious problem with oxyhemoglobin desaturation. This subgroup appeared to have fewer problems with the craniofacial skeletal morphology (PCs 1.1 [-0.524], 1.6[-0.530], and 1.7 [+0.569]). The adaptation of head posture was not seen in this group (PCs 2.1 [-0.551], 2.2 [-0.587]). The second subgroup, resulting from the third canonical correlation, was nonobese OSA patients with a problem of oxyhemoglobin desaturation. The adaptation of head posture (PCs 2.1 [+0.735], 2.2 [+0.726]) and atypical vertical and narrow anteroposterior dimension of craniofacial skeletal morphology was evident in this group (PCs 1.1 [+0.610] and 1.2 [+0.569]).

By using partial least squares analysis, Lowe et al⁵⁰ found that the aforementioned changes of head posture were not only related to the decreased minimal oxyhemoglobin saturation but also to the increased OSA severity. Our finding of increased OSA severity and changes of head posture in the third canonical correlation were confined only to the obese OSA group. In the second canonical correlation of the obese group, BMI was evidently related to the increased size of the tongue and the soft palate. This finding was consistent with the results previously reported from a 3dimensional computerized tomography study.⁵¹ In the nonobese OSA group, which had lower AHI, its second canonical correlation demonstrated that the relationship of OSA severity was to a greater extent due to skeletal elements and to a lesser extent to the hyoid bone position and upper airway soft tissue. However, as the association was approximately 52%, there must be other factors involved that influence the OSA severity, such as sleep position,⁵² atypical nocturnal activity of genioglossus,53 and loss of neuromuscular reflexes during sleep.54

Compared with advanced modern upper airway imaging (such as computerized tomography, magnetic resonance imaging, and videoendoscopy), cephalometric analysis, together with multivariate statistical analysis, seems to provide adequate information for diagnosis and treatment planning for OSA patients as well. This was evidently demonstrated by the consistency of our results with previous studies performed with more complicated imaging techniques. In conclusion, OSA subgroup characteristics, such as obesity and nonobesity, should be carefully taken into consideration for selection of treatment regimens chosen because of the differences in the interdependence of craniofacial morphology and the demographic characteristics.

CONCLUSIONS

This study illustrated the simultaneous relationship of selected demographic polysomnographic data and PCs of cephalometric variables in 57 obese and 43 nonobese OSA patients. Three canonical variables and their correspondents with different loadings were established differently for both OSA groups. A canonical correlation successfully clarified the complexity of simultaneous relationship of the relevant variables. This lays down a basis of understanding the complicated pathogenic components of obese and nonobese OSA patients. Therefore, the different morphologic components and their relevance to the diagnostic data obtained from sleep laboratories must be taken into consideration before treatment selection.

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