Assessment of Upper-Airway Configuration in Obstructive Sleep Apnea Syndrome With Computed Tomography Imaging During Müller Maneuver

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BACKGROUND: The purpose of this observational study was to investigate the relationship between upper-airway configuration assessed by CT imaging during the Müller maneuver state and the severity of obstructive sleep apnea syndrome (OSAS). **METHODS:** A total of 358 snoring subjects who underwent standard polysomnography and upper-airway configuration by using CT imaging were enrolled. According to the apnea-hypopnea index (AHI), subjects were classified into 4 groups: snoring group (simple snoring), $AHI < 5$; mild OSAS, $5 \leq AHI < 15$; moderate OSAS, $15 \leq AHI < 30$; and severe OSAS, $AHI \geq 30$. We also divided the upper airway into 3 parts, named the nasopharynx, oropharynx, and hypopharynx, from the CT scan and evaluated the minimal cross-sectional area (mCSA) and the shape of each airway level and calculated upper-airway length and distance from mandibular plane to hyoid bone (MPH). **RESULTS:** Multivariate logistic stepwise regression analysis identified body mass index (BMI), mCSA of nasopharynx, upper-airway length, and MPH as risk factors for the severity of OSAS. When subdivided for BMI and sex, upper-airway length was a risk factor for OSAS in non-obese ($BMI < 27 \text{ kg/m}^2$) and male subjects, and MPH was a risk factor only in obese ($BMI \geq 27 \text{ kg/m}^2$) subjects. Meanwhile, mCSA of nasopharynx was significantly associated with the severity of OSAS independent of BMI. **CONCLUSIONS:** Subjects with severe OSAS have more significant abnormalities of the upper airway. Obesity, mCSA of nasopharynx, upper-airway length, and MPH may contribute to the severity of OSAS. Obesity and sex should be taken into account when evaluating the abnormalities of upper-airway anatomy in snorers and patients with OSAS. *Key words:* obstructive sleep apnea syndrome; upper-airway configuration; CT; BMI; sex. [Respir Care 2016;61(12):1651–1658. © 2016 Daedalus Enterprises]

Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly prevalent disease that is characterized by repet-

itive episodes of partial or complete upper-airway obstruction. Snoring has always been considered as one of the cardinal symptoms of OSAS, and snorers have a high risk of developing OSAS¹ and may even be in the early stage of OSAS.

It has been suggested that anatomical abnormalities of the upper airway, including upper-airway collapsibility, length and size, alterations in craniofacial structure, and enlarge-

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ment of surrounding soft tissue structures (ie, tongue and lateral pharyngeal walls), play an important role in the development of OSAS,²⁻⁷ and many authors have examined the shape and minimal cross sectional area (mCSA) at different levels of the upper airway in the transverse field, since the recurrent collapse of the upper airway during sleep is one of the most important pathogeneses in OSAS.^{3,6-9} Moreover, researchers also have examined the influence of body mass index (BMI) and sex on the anatomy of the upper airway.^{3,10,11} It has been suggested that non-obese patients with OSAS may have a higher incidence of upper-airway abnormalities.^{3,11} Mayer et al³ found that in subjects with lower BMI, upper-airway abnormalities explain a major part of the variance in apnea–hypopnea index (AHI). However, Cosentini et al¹² reported that obese subjects with OSAS had a very small minimal cross-sectional area with magnetic resonance imaging during wakefulness. In addition, results from previous studies have shown that the upper-airway length was significantly longer in men, which could partially explain the predisposition of men to OSAS compared with women,^{10,13} and it was also found that an inferiorly positioned hyoid, evaluated by distance from mandibular plane to hyoid bone (MPH), was commonly associated with OSAS.^{4,6} These controversial results suggest that different anatomical or physiological mechanisms may play the major role in the propensity to apnea in apnea patients of different BMI or sex.

Although most studies have been carried out by using CT to determine upper-airway configuration, most of them used a small sample size and did not investigate the effects of upper-airway length and MPH on the severity of OSAS simultaneously. Because one cannot expect a single anatomical abnormality to explain all of the variance in sleep apnea, upper-airway length and MPH, which have been reported to play an important role in the pathophysiology of OSAS,^{3,5,7,14} should also be taken into account when evaluating the relationship of upper-airway configuration and the severity of OSAS. Moreover, CT scan with the Müller maneuver state, which involves maximal inspiration against a closed nose and mouth and can well identify sites of upper-airway obstruction and reveals OSAS severity,^{15,16} has great advantages in detecting sites of upper-airway obstruction.

In the present study, we evaluate the upper airway by CT scan with the Müller maneuver using the largest reported sample to date (358 subjects). We aim to investigate whether the severity of OSAS was associated with the structural changes of the upper airway induced by the Müller maneuver, even after stratification by BMI and sex of the subjects.

QUICK LOOK

Current knowledge

Anatomical abnormalities of the upper airway play an important role in the development of OSAS. Recurrent collapse of the upper airway during sleep induced by upper-airway abnormalities, including narrowing of the pharyngeal lumen and changing of pharyngeal shape, is one of the most important pathogeneses in OSAS, and BMI and sex have an effect on the anatomy of the upper airway.

What this paper contributes to our knowledge

Upper-airway abnormalities, including narrowing of nasopharynx, upper-airway length, and the distance from the mandibular plane to the hyoid bone, are likely to play an important physiopathogenic role in OSAS. Men have more upper-airway abnormalities, and obesity has a great effect on upper-airway length and the distance from the mandibular plane to the hyoid bone but not the area of the upper airway.

Methods

Subjects

Consecutive subjects who were referred to our sleep laboratory with a chief complaint of snoring from February 2013 to February 2015 were included to our study. Exclusion criteria were as follows: patients with asthma, COPD, cerebrovascular disease, symptomatic ischemic heart disease, congestive heart failure, chronic renal failure, hypothyroidism, and rheumatologic diseases according to self-reported medical histories. We also excluded patients with nasal, oral, pharyngeal, or mandibular diseases. Patients who had been previously diagnosed with or treated for OSA were also excluded. The final sample of this study comprised 358 subjects who met the inclusion criteria. Each subject had undergone both upper-airway CT scanning and a polysomnographic analysis (described below). This research was approved by institutional review board in the First Affiliated Hospital of Fujian Medical University.

Medical History and Anthropometric Measurements

Age, a detailed questionnaire on sleep symptoms, Epworth sleepiness scale, and history of alcohol consumption and smoking were recorded for all subjects. Body weight and height were measured without shoes and lightly clothed in the morning, and BMI was calculated as kg/m². Waist circumference was measured in the middle between the

12th rib and the iliac crest, and neck circumference was measured at the level of the laryngeal prominence by a measuring tape.

Polysomnography

Polysomnography (P Series Sleep System, Compumedics, Melbourne, Australia) was performed overnight between 10:00 pm and 6:00 am, and the following parameters were recorded simultaneously: electroencephalography, electrooculography, electromyography, air flow by nasal and oral thermistors, respiratory effort by thoracic and abdominal impedance belts, arterial oxyhemoglobin saturation by pulse oximetry, snoring by tracheal microphone, and changing of the body position during sleep by sensor. According to the criteria of American Academy of Sleep Medicine published in 2012,¹⁷ the polysomnography recordings were manually scored for sleep stages by a physician. Apnea was defined as decrements in air flow of $\geq 90\%$ from baseline for ≥ 10 s. Hypopnea was defined as a $\geq 30\%$ decrease in flow, lasting ≥ 10 s, accompanied by a $\geq 4\%$ oxyhemoglobin saturation (or followed by an arousal when OSAS was diagnosed by overnight polysomnography). The AHI was calculated as the number of apneas and hypopneas/h of polysomnographically recorded sleep time. The oxygen desaturation index was defined as the number of dips in S_{pO_2} of $\geq 4\%/h$ of polysomnographically recorded sleep time. Other polysomnographic parameters also included lowest O_2 saturation, mean nocturnal oxygen saturation (average S_{pO_2}), and the percentage of sleep time with $S_{pO_2} < 90\%$. Subjects were divided into 4 groups with respect to OSAS severity based on AHI: snoring group (simple snoring), $AHI < 5$; mild OSAS, $5 \leq AHI < 15$; moderate OSAS, $15 \leq AHI < 30$; and severe OSAS, $AHI \geq 30$. OSAS severity was defined as early OSAS when AHI was < 15 events/h, and advanced OSAS was defined as when it was ≥ 15 events/h.¹⁸

CT Evaluation

CT scan was used to measure anteroposterior and transverse diameters at the level of the nasopharynx (upper limit, cranial base; lower limit, tip of uvula), oropharynx (upper limit, tip of uvula; lower limit, tip of the epiglottis), and hypopharynx (upper limit, at the level of vallecula; lower limit, level of the cricoid cartilage) in the Müller maneuver state in all subjects. Slices in the axial plane, extending from the skull base to the hypopharynx, below the level of the cricoid cartilage, were collected in 5-mm intervals, with a total scan time of 10 s. All of the subjects remained awake in the supine position with the Frankfort plane perpendicular to the floor accompanied. A lateral scout view was first taken to determine and standardize the level of the scans during quiet tidal breathing (Fig. 1A).

Fig. 1. Computed tomography using a lateral scout view (A) was first used to determine and standardize the level of the scans during quiet tidal breathing, extending from the skull base to the hypopharynx, below the level of the cricoid cartilage. Upper airway length (UAL) and the distance from the mandibular plane to the hyoid bone (MPH) were obtained from the lateral scout view. B: Cross-sectional image of a subject at the level of the nasopharynx in the Müller maneuver state. C: Complete obstruction of the airway at the level of the nasopharynx in the Müller maneuver state.

Table 1. Anthropometric Characteristics and Polysomnography Parameters in All Subjects According to Obstructive Sleep Apnea Syndrome Status

	Snoring Group	Mild OSAS	Moderate OSAS	Severe OSAS	<i>P</i>
Subjects, <i>n</i>	37	50	71	200	
Sex, <i>n</i> (%)					
Male	51 (56.8)	36 (72.0)	65 (91.5)	181 (90.5)	< .001
Female	16 (43.2)	14 (28.0)	6 (8.5)	55 (9.5)	
Age, mean $\pm$ SD y	44.49 $\pm$ 14.47	46.94 $\pm$ 10.54	45.39 $\pm$ 10.77	45.52 $\pm$ 11.94	.80
Current smoking, <i>n</i> (%)	10 (27.0)	17 (34.0)	26 (37.1)	73 (37.2)	.67
Alcohol consumption, <i>n</i> (%)	1 (2.7)	4 (8.0)	7 (10.0)	42 (21.5)	< .001
BMI, mean $\pm$ SD kg/m ²	23.82 $\pm$ 3.20	25.30 $\pm$ 2.85	25.68 $\pm$ 2.35	28.03 $\pm$ 5.83	< .001
Neck circumference, mean $\pm$ SD cm	36.07 $\pm$ 3.56	37.67 $\pm$ 3.88	38.50 $\pm$ 2.95	40.09 $\pm$ 3.12	< .001
Waist circumference, mean $\pm$ SD cm	86.33 $\pm$ 9.34	90.36 $\pm$ 8.66	93.14 $\pm$ 7.58	98.11 $\pm$ 10.45	< .001
AHI, median (IQR) events/h	2.70 (0.80–4.15)	10.30 (7.95–12.10)	21.40 (19.10–24.50)	55.95 (44.63–66.70)	< .001
ODI, median (IQR) events/h	1.50 (0.65–2.60)	6.65 (3.78–8.33)	15.25 (9.10–20.50)	48.90 (32.80–64.35)	< .001
T90%, median (IQR) %	0.00 (0.00,0.06)	0.29 (0.03,1.40)	1.50 (0.26,4.09)	14.18 (3.68,27.99)	< .001
LaSO ₂ , median (IQR) %	90.00 (86.00–91.00)	85.00 (80.00–88.00)	80.00 (76.00–84.00)	67.00 (56.00–78.00)	< .001
Average S _{pO₂} , median (IQR) %	97.00 (95.00–97.00)	95.00 (94.00–96.00)	95.00 (93.00–96.00)	91.00 (87.00–94.00)	< .001
ESS score, mean $\pm$ SD	7.08 $\pm$ 4.34	8.44 $\pm$ 5.25	7.45 $\pm$ 5.62	10.11 $\pm$ 5.26	< .001

OSAS = obstructive sleep apnea syndrome

BMI = body mass index

AHI = apnea-hypopnea index

IQR = interquartile range

ODI = oxygen desaturation index

T90% = percentage of total sleep time spent with S_{pO₂} < 90%LaSO₂ = lowest O₂ saturation

ESS = Epworth sleepiness scale

The mCSA within the nasopharynx, oropharynx, and hypopharynx regions (mCSA-nasopharynx, mCSA-oropharynx, and mCSA-hypopharynx) was obtained through measuring anteroposterior and transverse, and the shape at each mCSA level was expressed as the ratio of anteroposterior to transverse (anteroposterior/transverse nasopharynx, anteroposterior/transverse oropharynx, and anteroposterior/transverse hypopharynx) in the Müller maneuver state (Fig. 1, B and C). Upper-airway length was defined as the vertical distance from the hard palate to the hyoid in the mid-sagittal plane. We also calculated the MPH. Upper-airway length and MPH were obtained from the lateral scout view during quiet respiration within the first 5 s (Fig. 1A). We did not recognize any problematic images (eg, not in the neutral anatomical position) while reviewing the CT scan. Every subject was taught how to perform the Müller maneuver several times until they could perform the standard maneuver to avoid bias. All of the measurements were done manually by one clinician, who was blinded to the polysomnography data.

Statistical Analysis

All statistical analysis was performed by using SPSS 17.0 for Windows (SPSS, Chicago, Illinois). Before analysis, all variables were examined for normal distribution. Normally distributed, skewed, and categorical data are expressed as mean $\pm$ SD, median (interquartile range), and *n* (%), respec-

tively. Then normally distributed continuous variables were analyzed by using one-way analysis of variance for multiple-group comparison. Skewed data were compared by using Kruskal-Wallis H (K). All categorical variables were analyzed by the chi-square test or Fisher exact test. In view of the influence of BMI and sex on the anatomy of the upper airway, the correlation between AHI and clinical, CT data was evaluated in the overall population and in the different groups of BMI (using the cut-off point of < 27 and $\geq$ 27 kg/m²) and sex by Spearman's correlation test. Subjects were divided into early OSAS and advanced OSAS based on different treatment modalities, and stepwise logistic regression analyses were performed with the severity of OSAS as the dependent variable in the overall population and in the different groups of BMI and sex. Differences were considered significant when *P* was < .05.

Results

A total of 358 subjects were evaluated in this study. Seventy-two percent of them were male, with the mean age of all subjects 45.6 $\pm$ 11.8 y and the mean BMI 26.75 $\pm$ 4.95 kg/m². Based on the severity of OSAS, all of the subjects were divided into early OSAS (*n* = 87, 24.3%) and advanced OSAS (*n* = 271, 75.7%).

Anthropometric characteristics and polysomnography parameters of subjects are summarized in Table 1. There were no significant differences among the 4 groups with

Table 2. Upper-Airway Measurements in All Subjects According to the Presence of Obstructive Sleep Apnea Syndrome and Its Severity

	Snoring Group	Mild OSAS	Moderate OSAS	Severe OSAS	<i>P</i>
T-NP, median (IQR) cm	1.55 (1.23–2.00)	1.41 (1.16–1.72)	1.45 (0.98–1.77)	0.98 (0.66–1.45)	< .001
AP-NP, median (IQR) cm	0.85 (0.74–1.03)	0.74 (0.56–0.95)	0.70 (0.56–0.96)	0.66 (0.47–0.89)	< .001
T-OP, median (IQR) cm	2.44 (1.85–3.08)	2.39 (1.99–2.89)	2.15 (1.71–2.76)	1.83 (1.36–2.43)	< .001
AP-OP, median (IQR) cm	1.22 (0.83–1.55)	1.28 (1.00–1.60)	1.27 (1.03–1.50)	1.22 (0.94–1.59)	.96
T-HP, median (IQR) cm	0.90 (0.40–1.17)	1.08 (0.43–1.26)	0.70 (0.23–1.22)	0.75 (0.23–1.17)	.14
AP-HP, median (IQR) cm	1.50 (0.92–1.90)	1.59 (0.51–1.94)	1.31 (0.52–2.01)	1.23 (0.28–1.91)	.21
mCSA-NP, median (IQR) cm ²	1.25 (0.93–1.98)	1.13 (0.64–1.79)	0.94 (0.62–1.49)	0.68 (0.35–1.05)	< .001
mCSA-OP, median (IQR) cm ²	2.93 (1.64–4.36)	3.12 (2.31–4.14)	2.70 (2.00–3.76)	2.25 (1.44–3.36)	.01
mCSA-HP, median (IQR) cm ²	1.10 (0.37–1.94)	1.71 (0.21–2.39)	0.90 (0.13–2.39)	1.06 (0.07–2.04)	.19
AP/T-NP, median (IQR)	0.54 (0.45–0.73)	0.50 (0.37–0.75)	0.56 (0.41–0.70)	0.64 (0.47–0.94)	.01
AP/T-OP, median (IQR)	0.38 (0.49–0.63)	0.52 (0.42–0.67)	0.54 (0.43–0.77)	0.64 (0.48–0.93)	< .001
AP/T-HP, median (IQR)	1.65 (1.24–2.12)	1.44 (1.33–1.85)	1.73 (1.32–2.00)	1.46 (1.08–1.93)	.16
UAL, mean $\pm$ SD cm	6.71 $\pm$ 1.28	6.90 $\pm$ 0.77	7.16 $\pm$ 0.67	7.86 $\pm$ 0.99	< .001
MPH, mean $\pm$ SD cm	1.70 $\pm$ 1.04	1.57 $\pm$ 0.67	1.71 $\pm$ 0.65	2.44 $\pm$ 0.82	< .001

IQR = interquartile range

T-NP = transverse diameter at the mCSA level of nasopharynx

T-OP = transverse diameter at the mCSA level of oropharynx

T-HP = transverse diameter at the mCSA level of hypopharynx

AP-NP = anteroposterior diameter at the mCSA level of nasopharynx

AP-OP = anteroposterior diameter at the mCSA level of oropharynx

AP-HP = anteroposterior diameter at the mCSA level of hypopharynx

mCSA-NP = minimal cross sectional area within the nasopharynx region

mCSA-OP = minimal cross sectional area within the oropharynx region

mCSA-HP = minimal cross sectional area within the hypopharynx region

AP/T = anteroposterior/transverse axis ratio

UAL = upper-airway length

MPH = distance from the mandibular plane to the hyoid bone

respect to age and current smoking. Polysomnographic parameters, including lowest O₂ saturation and average S_{PO₂}, decreased significantly with an increase in OSAS severity, whereas alcohol consumption, BMI, neck circumference, waist circumference, AHI, oxygen desaturation index, and percentage of sleep time with S_{PO₂} < 90% increased with OSAS severity.

Table 2 presents upper-airway measurements in the Müller maneuver state. No significant differences were observed in terms of anteroposterior oropharynx, transverse hypopharynx, anteroposterior hypopharynx, and mCSA-hypopharynx among groups. Among the subjects with severe OSAS, transverse nasopharynx, anteroposterior nasopharynx, and transverse oropharynx were 0.98, 0.66, and 1.83 cm, decreased significantly when compared with the snoring group ($P < .001$, $P < .001$, and $P < .001$, respectively). The mCSA-nasopharynx and mCSA-oropharynx among subjects with severe OSAS were smaller when compared with the snoring group (0.68 cm² vs 1.25 cm² [$P < .001$] and 2.25 cm² vs 2.93 cm² [$P < .001$], respectively). Considering the anteroposterior/transverse ratio at the level of nasopharynx and oropharynx, the severe OSAS group tended to present a more spherical shape at the level of nasopharynx and of oropharynx. In addition, a strong positive association was observed between OSAS severity

and the indices of upper-airway length and MPH (both $P < .001$).

Table 3 summarizes the associations between upper-airway measurements and polysomnographic parameters in the overall population and in the different groups of BMI and sex. There were significant correlations between AHI and mCSA and the shape of the upper airway, including mCSA-nasopharynx, mCSA-oropharynx, mCSA-hypopharynx ($r = -0.366$, -0.181 , and -0.140 ; $P < .001$, $P < .001$, and $P < .001$, respectively). We also observed positive correlations between AHI and the upper-airway length and MPH ($r = 0.521$ and 0.481 ; both $P < .001$). Additionally, Spearman's correlation also revealed a significant association between AHI and sex and BMI ($r = 0.242$ and 0.484 ; both $P < .001$). Afterwards, in the BMI class < 27 kg/m², mCSA-nasopharynx, mCSA-oropharynx, upper-airway length, MPH, sex, and BMI were significantly correlated with AHI. In the BMI class ≥ 27 kg/m², mCSA-nasopharynx, upper-airway length, MPH, sex, and BMI were significantly correlated with AHI. In the subgroup of males, mCSA-nasopharynx, mCSA-oropharynx, mCSA-hypopharynx, upper-airway length, MPH, and BMI were significantly correlated with AHI, whereas only age, BMI, and mCSA-nasopharynx were significantly correlated with AHI in the group of females.

Table 3. Spearman's Rank Correlation Coefficients Between Polysomnography Parameters, Anthropometric Characteristics, and Upper-Airway Measurements

	r				
	Total (N = 358)	BMI < 27 (n = 209)	BMI ≥ 27 (n = 147)	Female (n = 55)	Male (n = 303)
Age	−0.067	0.006	−0.071	0.313*	−0.082
Sex	0.242*	0.312*	0.175*	NA	NA
BMI	0.484*	0.246*	0.357*	0.555*	0.461*
mCSA-NP	−0.366*	−0.342*	−0.299*	−0.340*	−0.352*
mCSA-OP	−0.181*	−0.157*	−0.145	−0.084	−0.181*
mCSA-HP	−0.140*	−0.093	−0.101	−0.090	−0.133*
UAL	0.521*	0.490*	0.524*	0.265	0.498*
MPH	0.481*	0.387*	0.535*	0.180	0.480*

* $P < .05$.

NA = not applicable

BMI = body mass index

mCSA-NP = minimal cross sectional area within the nasopharynx region

mCSA-OP = minimal cross sectional area within the oropharynx region

mCSA-HP = minimal cross sectional area within the hypopharynx region

AP/T-NP = anteroposterior/transverse axis ratio of nasopharynx

AP/T-OP = anteroposterior/transverse axis ratio of oropharynx

AP/T-HP = anteroposterior/transverse axis ratio of hypopharynx

UAL = upper-airway length

MPH = distance from the mandibular plane to the hyoid bone

For the overall population, multivariate stepwise logistic regression analyses showed the following factors as determinants of the severity of OSAS: BMI, mCSA-nasopharynx, upper-airway length, and MPH. In the group with a BMI < 27 kg/m², sex, mCSA-nasopharynx, and upper-airway length were associated with the severity of OSAS, whereas mCSA-nasopharynx and MPH emerged in the group with a BMI ≥ 27 kg/m². In the subgroup of males, anteroposterior/transverse oropharynx and upper-airway length were the independent variables for the severity of OSAS, whereas only age and BMI were significantly correlated with AHI in the group of females (Table 4).

Discussion

The present study provides evidence that there were significant correlations between mCSA and the shape of the upper airway and the severity of OSAS in the Müller maneuver state. In the logistic regression model, besides BMI, mCSA-nasopharynx, upper-airway length, and MPH were found to be significant risk factors for OSAS. Meanwhile, when subjects were classified according to BMI and sex, multivariate logistic stepwise regression analysis revealed that upper-airway length was a significant risk factor only in non-obese male subjects with OSAS, and MPH was a significant factor in obese subjects. Another important new finding was that subjects were commonly characterized by upper-airway narrowing at the level of nasopharynx independent of BMI.

Table 4. Multivariate Stepwise Logistic Regression Analysis Models for Different Groups According to Severity of Obstructive Sleep Apnea Syndrome

Variable	P	Odds Ratio	95% CI
Overall			
BMI	< .001	1.246	1.114–1.394
mCSA-NP	.025	0.641	0.435–0.945
UAL	.002	1.644	1.198–2.256
MPH	.01	1.640	1.109–2.424
BMI < 27 kg/m ²			
Sex	.047	2.636	1.014–6.856
mCSA-NP	< .001	0.628	0.411–0.958
UAL	.002	2.019	1.283–3.178
BMI ≥ 27 kg/m ²			
mCSA-NP	.048	0.481	0.233–0.994
MPH	.001	4.882	1.898–12.560
Female			
Age	.02	1.079	1.014–1.148
BMI	.004	1.375	1.108–1.706
Male			
AP/T-OP	.008	6.148	1.607–23.517
UAL	< .001	2.428	1.593–3.701

BMI = body mass index

mCSA-NP = minimal cross sectional area within the nasopharynx

UAL = upper-airway length

MPH = distance from the mandibular plane to the hyoid bone

AP/T-OP = anteroposterior/transverse axis ratio of oropharynx

The mechanisms responsible for upper-airway collapse and apnea were incompletely understood in snorers and patients with OSAS. Previously, it had been reported that upper-airway collapse induced by upper-airway abnormalities, including narrowing of the pharyngeal lumen and changing of pharyngeal shape, leads to snoring and apnea during sleep^{3,8,19,20}; however, few researchers had focused on mCSA and the shape of the upper airway in the Müller maneuver state. It is believed that the the Müller maneuver, a method to simulate upper-airway collapsibility under intraluminal pressure during sleep, has been validated in sleep apnea, and collapse of the pharynx induced by the Müller maneuver is highly related to severity of OSAS.^{15,18,21} In the present study, mCSA of nasopharynx, oropharynx, and hypopharynx all had a negative correlation with OSAS severity in the Müller maneuver state, and mCSA of nasopharynx was an independent variable for OSAS following multiple logistic regression analyses in both obese and non-obese subjects. Our results were similar to those of smaller studies using CT to identify change in the upper airway.^{8,20} However, some studies did not find any significant differences in the upper-airway area between OSAS and control subjects,^{3,7} even those grouped by BMI.³ In addition, we also found in our study that a more spherical shape of the oropharynx plays a more important role in the development of OSAS in male subjects

with an odds ratio of 6.148 (95% CI 1.607–23.517). Mayer et al³ showed that the shapes of the oropharynx and hypopharynx were more spherical in the higher BMI group, which could not be found in this study. The influence of the breathing cycle and state may partly account for the inconsistent conclusion.

In this study, we also have demonstrated that upper-airway length and MPH were significantly correlated with AHI, as expected. Some researchers have elucidated the importance of upper-airway length in potentially explaining pharyngeal collapse.^{5,7,14} Sutherland et al¹⁴ investigated the effect of weight loss on upper-airway length in obese men and suggested that reduced upper-airway length was associated with a greater improvement in OSAS. The correlation between upper-airway length change and its collapsibility could be explained based on Bernoulli's law, which states that an inviscid liquid flowing through a tube is susceptible to an increase in velocity and decrease in pressure.²² According to the rules of buckling of cylindrical shells,²³ upper-airway length would increase, and the upper airway would be increasingly prone to collapse because it lacks rigid bony structures. Therefore, it seems that upper-airway length is a possible mechanism contributing to increased upper-airway collapsibility in patients with OSAS. Our data also showed that the upper-airway length might be a dominant contributing factor for obstructive sleep apnea in men or non-obese patients. These findings were in accordance with previous studies in subjects with OSAS^{5,7} but were discussed here for the first time, to our knowledge, in non-obese subjects with OSAS.

Another finding in this study was that MPH was an independent variable for significant OSAS with an odds ratio of 1.640 (95% CI 1.109–2.424) in all subjects and 4.882 (95% CI 1.898–12.560) in obese subjects. The hyoid bone, which serves as anchorage for the tongue muscles, affects the patency of the hypopharyngeal airway, and inferiorly positioned hyoid bone in OSAS has been well documented.^{4,6,20} In one study, it was found that the vertical distance of the hyoid position decreased after weight loss, suggesting that this phenomenon results from a lessening of downward pressure due to a reduction in excess pharyngeal tissues.¹⁴ In agreement with the previous reports, our study also indicated a more inferior hyoid bone position likely to play an important physiopathogenic role in OSAS, especially in obese patients.

Previous studies have also reported that cephalometric features and the upper-airway abnormalities were more important risk factors for OSAS in non-obese compared with obese subjects.^{3,24,25} However, in the study of Tangsgorn et al,²⁶ subjects with OSAS displayed aberrations of cervico-craniofacial and upper-airway soft tissue morphology irrespective of the BMI. These conflicting results suggest that the influence of obesity on patient abnormalities remains to be established. The results of our study

showed that abnormalities such as narrowing of the pharyngeal lumen were found in obese and non-obese subjects regardless of BMI, whereas upper-airway length was the major determinant in non-obese subjects and MPH in the obese group. It has been speculated that these abnormalities possibly imply a genetic predisposition to OSAS in such patients.³ Furthermore, we also noted a sex difference in the upper-airway abnormalities and found that men had more predisposing factors than did women, including a more spherical shape of the oropharynx and more inferiorly positioned hyoid bones, which might partly explain why being male is a major risk factor for OSAS. These findings in our study suggest that the etiology of OSAS is multifactorial, and obesity, sex, and subtle abnormalities in upper-airway configuration are important factors in its pathogenesis.

The present study clearly has several limitations. First, the CT scan was conducted on awake subjects, whereas OSAS is a dynamic phenomenon occurring as patients are asleep. However, it is not practical to perform CT imaging on sleeping patients. Thus, we evaluated upper airways in the Müller maneuver state, which was a method to simulate upper-airway collapsibility during sleep.²¹ Second, from an ethical viewpoint, CT in OSAS diagnosis puts patients at risk of radiation exposure compared with other clinically used diagnostic methods, such as nasopharyngoscopy and magnetic resonance imaging. However, CT scanning had advantages, including providing multiple-level, rapid-sequence scans, sensitivity to both soft tissue and bony landmarks, the ability to combine it with polysomnography, and the noninvasive nature of the technique. Third, we only selected a few of the potentially important variables that may determine the impact of airway configuration on sleep apnea severity instead of examining all of the parameters of airway configuration. Other measurements that may be important include soft-tissue thickness around the airway, tongue length, and others. We chose measurements that were believed to be simple and intuitively correlated to the severity of sleep apnea to avoid problems with biases related to repeated measures.

Conclusions

Upper-airway abnormalities, including narrowing of the nasopharynx, upper airway-length, and MPH are more likely to play a more important physiopathogenic role for OSAS in the overall population following multiple logistic regression analyses. Our study also suggests that men have more upper-airway abnormalities and that obesity has a great effect on upper-airway length and the distance from mandibular plane to the hyoid bone but not the area of the upper airway. The precise mechanism underlying the association with obesity, sex, and subtle abnormalities in upper-airway configuration requires further clarification.

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