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Clinical Predictors in Obstructive Sleep Apnea Patients with Computer-Assisted Quantitative Videoendoscopic Upper Airway Analysis

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Aim: **To identify the clinical predictors and assist surgeons in their clinical management of obstructive sleep apnea (OSA). A prospective study with a new approach to analyze the static and dynamic upper airway morphology between patients with OSA and normal subjects.** ***Method:*** **Quantitative computer-assisted videoendoscopy (validated with upper airway magnetic resonance imaging) was performed in 49 (43 males, 6 females) patients with OSA and compared with 39 (22 males, 17 females) controls (apnea-hypopnea index [AHI] < 5). Absolute cross-sectional areas and transverse and longitudinal diameters at the retropalatal and retrolingual levels were measured during end of quiet respiration and during Mueller's maneuver in the erect and supine positions, allowing us to study static and dynamic morphology (collapsibility) of the upper airway. Three thousand seven hundred forty-four (3,744) parameters were analyzed.** ***Results:*** **In males, retropalatal and retrolingual areas during Mueller's maneuver in the supine position of 0.7981 cm^2 (relative operating characteristics [ROC] = 0.9284, positive pressure ventilation [PPV] = 86.05%, negative pressure ventilation [NPV] = 84.62%) and 2.0648 cm^2 (ROC = 0.8183, PPV = 76%, NPV = 83.33%), respectively, were found to be good predictors/cut-off values for OSA. The retropalatal area measured in the supine position (AS1 mol/L) and collapsibility of the retropalatal area in the supine position (CAS1) were found to have significant correlations with severity of OSA. In females, the areas measured during Mueller's maneuver in the supine position of 0.522 cm^2 at the retropalatal level (ROC = 1, 100% PPV and NPV) and the transverse diameter at the retrolingual level during erect Mueller's maneuver of 1.1843 cm (ROC = 0.9056, PPV = 100%, NPV = 83.33%) were found to be predictive. All measurements at the retropalatal level and in the supine position had higher predictability. Area measurements obtained during Muller's maneuver were more predictive (ROC > 0.9910) than resting measurements (ROC > 0.8371). Several sex and anatomic-site specific formulas with excellent predictability (ROC close or equal to 1) were also devised.** ***Conclusion:*** **Upper airway Mueller's studies are predictive and useful (independent samples t test/Mann-Whitney *U* test, ROC) in identifying patients with OSA. With these sex and anatomic-site specific OSA predictors/formulas and this innovative clinical method, we hope to assist other surgeons with quantitative clinical diagnosis, assessment, surgical planning, and outcome assessment tools for OSA patients.** ***Key Words:*** **Obstructive sleep apnea, computer-assisted quantitative video endoscopic analysis, OSA predictors, Mueller's study.**
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INTRODUCTION

Obstructive sleep apnea (OSA) is a common disease, which is estimated to affect up to 2% of middle-aged women and 4% of middle-aged men.[1] Various attempts have been made to obtain predictive indicators of OSA, ranging from clinical predictors using body mass index (BMI),[1] Malampatti score[2] and tonsil size to lateral cephalometric measurements,[3,4] and nasopharyngoscopic assessment with or without Mueller's maneuver. Nasopharyngoscopy is a widely available technique commonly performed by otolaryngologists to evaluate the upper airway. This technique is easily performed in the outpatient setting and does not involve radiation exposure. Nasopharyngoscopy permits direct observation of the dynamic appearance of the pharynx and has been used in a number of research studies to evaluate the physiologic changes in a hypotonic airway in patients with OSA. Nasopharyngoscopy with Mueller's maneuver is an ideal modality to

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examine dynamic changes in upper airway caliber, and it can be used to determine the extent of retropalatal or retroglossal obstruction. The Mueller's maneuver is thought to simulate the upper airway collapse that occurs during apnea but is performed in wakefulness as the patient voluntarily inspires against a closed mouth and occluded nose.

Although the degree of obstruction during Mueller's maneuver may not be the same as during an apneic episode,[5] it provides information on the intrinsic soft tissue tone and collapsibility, which we believe bears a correlation to the level and extent of upper airway collapse. On this basis, several studies have been performed to evaluate OSA patients for suitability for uvulopalatopharyngoplasty using endoscopy with Mueller's maneuver. The methods of assessment in these early studies were all nonquantitative, relying on a subjective grading system or an eyeballing estimation, which probably contributed to variable results. In this study, a quantitative endoscopic method was applied to assess both OSA patients and normal subjects. This uses calibration and allows actual measurements in metric units and was validated against magnetic resonance imaging (MRI) measurements. Quantitative computer-assisted digital-imaging videoendoscopic upper airway analysis would enable surgeons to accurately quantify the dimensions, configurations, sites of obstruction, and collapsibility of upper airways. The results have enabled surgeons to characterize the static and dynamic morphology of the subjects' upper airway and to derive reliable indicators to predict OSA.

MATERIALS AND METHOD

Subjects All subjects, including subjects with suspected OSA (referrals from clinic) and healthy subjects (healthy volunteers without OSA symptoms), were randomly seen in our OSA clinic. All the bio-data of these subjects, including age, sex, height, weight, BMI, and neck circumference were recorded together with Epworth Sleepiness Scales into the OSA database. All subjects had their quantitative computer-assisted digital-imaging upper airway videoendoscopic examinations and measurements performed by surgeons in the first clinic visit within the same day. Overnight sleep studies (polysomnography [PSG]) were scheduled for all subjects within 2 weeks from their first clinic visit. Eighty-eight subjects entered this prospective study, 49 patients with OSA proven by PSG and 39 normal subjects without any daytime symptoms and with normal PSG (apnea-hypopnea index [AHI] < 5) and lowest oxygen saturation greater than 90%. Those control subjects recruited with sleep study of AHI equal or greater than 5 and with a lowest oxygen saturation of less than 90% were excluded from the control group. Subsequently, PSG data and video-endoscopic analysis results were collated and added to the database before analysis.

Polysomnography

PSG was performed over 1 night on all subjects. It included electroencephalogram (C3/A2, C4/A1, O2/A1), submental electromyogram (EMG), anterior tibialis EMG, electrocardiogram, thoracoabdominal motion, oronasal airflow (expired CO_2), and arterial oxygen saturation with pulse oximetry. The studies were scored manually, and the total AHI was calculated for that night. Obstructive apnea was defined as the cessation of airflow for at least 10 seconds accompanied by ongoing respiratory efforts. Hypopnea was defined as a reduction in airflow of at least 50% for at least 10 seconds accompanied by reduction in respiratory effort and by an arousal or an arterial oxygen desaturation of at least 3%.

Quantitative Computer-Assisted Digital-Imaging Videoendoscopic Assessment

Endoscopic examination of the subjects' upper airway were carried out using a nasopharyngoscope (Olympus ENF Type T3, Tokyo, Japan), with a calibrator (known dimension of 5 mm with the tip open) inserted through the instrument port and placed at the levels of interest. Subjects were allowed to perform/practice Mueller's maneuver until they were comfortable before the procedure started. The examination began with introduction of a lubricated nasopharyngoscope, and the entire upper airway was examined, with emphasis placed on the levels of obstruction. The calibrator was then slowly introduced through the instrument port and placed at the desired level. When the calibrator extends beyond the tip of the scope and within the field of video capture, the calibrator is fully open and brought to the level to be studied (retropalatal or retrolingual levels). Once the desired level was reached with calibrator, the surgeon performing the procedure would take note of the lengths of calibrator and scope inserted. In addition, anatomic landmarks were also used to guide the positioning of the calibrator at these two levels. The uvula was used as the landmark for the retropalatal level, and the tip of the epiglottis was used as the anatomic landmark for the retrolingual level. The purpose of these measures was to ensure the consistent positions of the calibrator in airway measurements during both the resting phase and Mueller's maneuver.

A video record of the entire examination was made, which included quiet respiration and Mueller's maneuver, at both erect and supine positions. Images of upper airways at maximal collapse were captured using a videocapture card (InterVideo WinProducer Version 2.0, Intervideo, Fremont, CA) and digital imaging software (JasCapture Version Shareware 2.0, JASC, Minneapolis, MN) equipped in the computer. Digital measurement software (Bersoft Image Measurement 1.0, Bersoft Inc, Ontario, Canada), which allowed the computer to generate the dimensions (transverse and longitudinal dimensions, surface areas) and calculate the collapsibility of obstructive sites of the upper airway, was employed. The actual dimensions were obtained by comparing the calibrator (5 mm) with these videoendoscopic images. Measurements were taken during the end of quiet respiration, during Mueller's maneuver, and in the erect and supine positions at two levels, namely the retropalatal and retrolingual levels (8 images per patient, as shown in Fig. 1). There was a minimum degree of subjectivity observed while outlining of the images of upper airway. Collapsibility was calculated by dividing the difference in measurement obtained between quiet respiration and during Mueller's maneuver with the original measurement obtained during

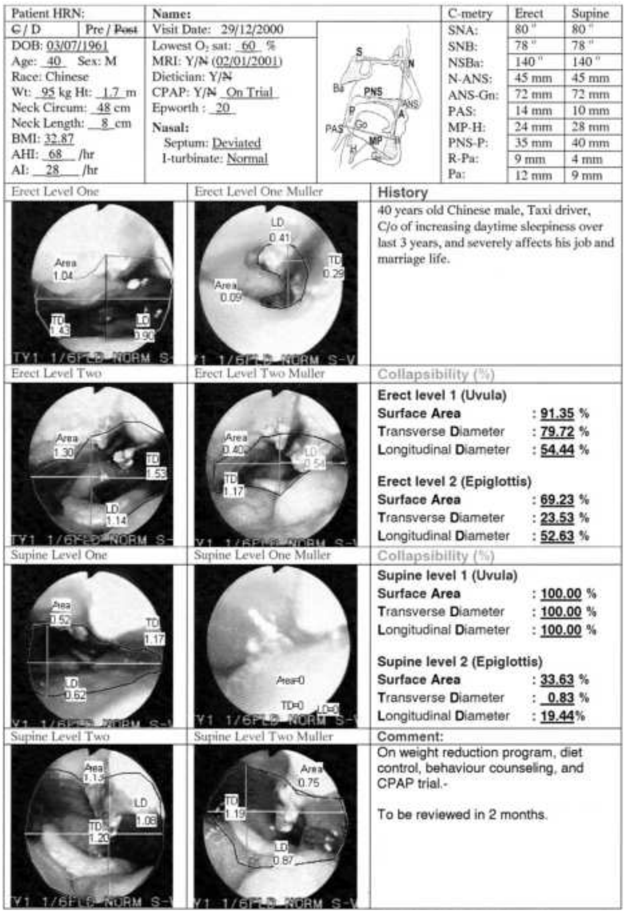


Fig. 1. Clinical summary and measurement data.

quiet respiration and expressed in terms of percentages. All measurements and calculated information (3,744 parameters) were subsequently transferred to our OSA database together with other data for further analysis.

Validation of Videoendoscopic Measurement

This new clinical method[6] was validated in our pilot study; a subsequent larger study included 45 subjects. This method is conducted in a blinded fashion (independent measurements of upper airway of 45 subjects obtained by surgeons and radiologists). Videoendoscopic examinations were performed for all subjects in the initial clinic visit, and the upper airway measurements were obtained within the same day by surgeons independently in the clinic. MRI scans were scheduled for all subjects with MRI upper airway measurements obtained by radiologists independently within 1 week of the initial clinic visit. These two sets of videoendoscopic and MRI measurement were subsequently collated, compared, and analyzed at the end of this study.

The videoendoscopic measurements were validated (Fig. 2) by comparing videoendoscopic measurements of the patients during quiet respiration (supine) with upper airway MRI scans (supine, quiet respiration) at both retropalatal and retrolingual levels. Two videoendoscopic images per patient, with a total 90 images, were compared

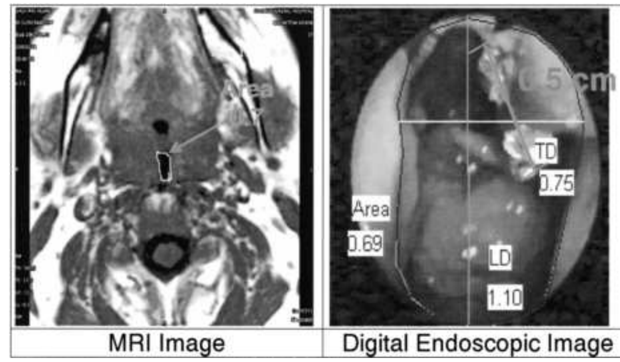


Fig. 2. Measurements validation. Comparing the area measurement between the upper airway magnetic resonance image (MRI) and digital endoscopic image at the identical level of upper airway.

with MRI scans. Once these two images were validated by MRI scans, we could assume (extrapolate) the remaining videoendoscopic images (Mueller's maneuver, Fig. 3, or erect position) to have the identical level of accuracy. The percentage accuracy (Fig. 4) was found to be 92.52% at the retropalatal level and 92.34% at the retrolingual level. These results indicate that this method of measurement gives consistently accurate upper airway measurement results.

Data Analysis

Statistically significant ($P < .05$) parameters and indices between OSA and normal subjects within sexes were determined using independent samples t test/Mann-Whitney *U* test. Receiver operating characteristics (ROC) curves were used to derive the predictive values of various parameters for OSA. Logistic regression was used to derive these predictive modeling/formulas.

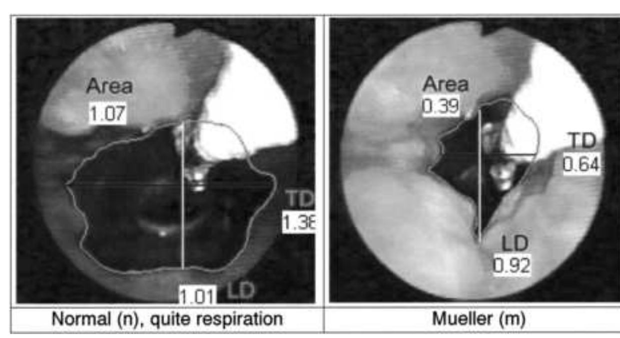
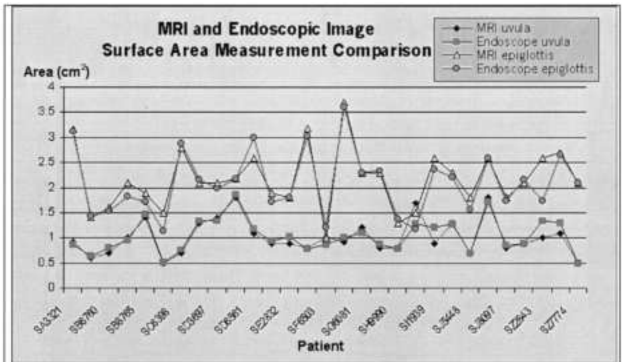


Fig. 3. Example of calculation of collapsibility:

$$\text{Area collapsibility} = \frac{\text{Area(n) - Area(m)}}{\text{Area(n)}} = \frac{1.07 - 0.39}{1.07} = \mathbf{63.56\%}$$

Transverse diameter and longitudinal diameter collapsibilities are similarly calculated.



Surface area measurements of MRI and Endoscopic images were plotted against 45 patients, at uvula and epiglottis levels in supine position.

Hence, 90 pairs of image measurements were captured. The surface area measurements of Digital Endoscopic images (D.I.) were compared with the MRI measurements in each pair. The above chart has shown the close proximity between two methods of measurements.

Difference (cm^2)	Level 1	Level 2
<= 0.5	**100 %**	**95.6 %**
<= 0.4	**97.8 %**	**91.1 %**
<= 0.3	**93.3 %**	**77.8 %**

Fig. 4. Quantitative precision (magnetic resonance imaging [MRI] vs. DI).

RESULTS

There were 49 (43 males, 6 females) patients with OSA and 39 (22 males, 17 females) control subjects (PSG AHI < 5). Table I shows the nomenclature for the naming convention of the variables of this study. For example, AE1 M means the cross-sectional area measured at retropalatal level at erect position during the Mueller's maneuver. Entries without the letter M indicate the measurement obtained during quiet respiration. Table II gives the descriptive statistics with comparisons between the OSA patients and controls within sex, with significant differences ($P < .05$) between the two groups in bold. For both sexes, neck circumference, neck length, AE1 M, AE2 M, AS1, AS1 M, AS2 M, TDE1 M, TDE2 M, TDS1 M, TDS2 M, LDE1 M, LDS1 M, CAE1, CAE2, CAS1, CAS2, CTDE1, CTDE2, CTDS1, CTDS2, CLDE1, CLDS1, weight, and BMI were significantly different between controls and OSA patients. Epworth Sleepiness Scale, age, height, TDS1, TDS2, LDS2 M, TD/LD E1, and TD/LD S1 were also significantly different for the males only.

ROC curves were used to determine the parameters that were good predictors (ROC > 0.7, maximum ROC $=$ 1) of OSA (Table III) (ROC > 0.7 are in bold). For both sexes, age, weight, Epworth score, BMI, neck circumference and length, AE1 M, AE2 M, AS1 M, AS2 M, TDE1 M, TDE2 M, TDS1, TDS1 M, TDS2 M, LDS1 M, CAE1, CAE2, CAS1, CAS2, CTDE1, CTDE2, CTDS1, CTDS2, CLDE1 and CLDS1 gave ROC greater than 0.7. For female patients, AE1, AS1, LDE1 M, LDE2 M, LDS1, CLDE2 and CLDS2 also gave ROC greater than 0.7, whereas for the males, only TD/LD S1 gave ROC greater than 0.7.

For each of the parameters that was found to be a good predictor for OSA, a cut-off value could be calculated to provide an indication of the likelihood of OSA. To simplify the large number of statistically significant parameters and enable ease of use as clinical predictors, one single parameter for each level was chosen. In Table III, for males, AS1 M at less than 0.7981 cm^2 was chosen—because it has the highest ROC (0.9284), with an excellent positive predictive value of 86.05% and negative predictive value of 84.62%—to be the single predictor for OSA at retropalatal level. For the retrolingual level, AS2 M less than 2.0648 cm^2 was chosen because it has the highest ROC value (0.8183) with positive predictive value of 76% and negative predictive value of 83.33% (Table IV).

In males, indices obtained during Mueller's maneuver and thus as calculated collapsibility were more predictive (ROC $>$ 0.9910) than resting/static area measurements (ROC $>$ 0.8371). This study compared the predictive value of anatomic parameters (both at rest and during Mueller's maneuver) obtained between erect and supine positions. In the erect position, the ROC of measurements of resting areas was 0.7104, and the ROC of measurements of areas during Mueller's maneuver was 0.8748. In the supine position, the ROC of measurements of resting areas was 0.7722, and the ROC of measurements of areas during Mueller's maneuver was 0.9759. In other words, the measurement of upper airway areas in the supine position had a higher predictive value for OSA than in the erect position for measurements taken at rest and during Mueller's maneuver.

For females, there were many parameters and indices with very high ROC, positive predictive value (PPV), and negative predictive value (NPV) values, but again, the large number of significant parameters were simplified. AS1 M less than 0.522 cm^2 at the retropalatal level gave a ROC of 1, and 100% PPV and NPV was selected. For the retrolingual level, TDE2 M less than 1.1843 cm with an ROC of 0.9056, a PPV of 100%, and an NPV of 83.33% was selected (Table IV).

In contrast with the results for male subjects, the indices obtained during Mueller's maneuver and hence collapsibility were equally predictive (ROC $=$ 1) when

TABLE I.
Nomenclature.

A	Area
TD	Transverse diameter
LD	Longitudinal diameter
E	Erect position
S	Supine position
Level 1	Retropalatal level
Level 2	Retrolingual level
M	Mueller manouvre
C	Collapsibility
OSA	Obstructive sleep apnea
ROC	Relative operating characteristics
CAM	Computer-assisted quantitative videoendoscopic analysis

TABLE II.
Descriptive OSA Data

Parameters	Males Control	Males OSA	Males *p* Value	Females Control	Females OSA	Females *p* value
Neck circumference cm	**37.18 (2.15)**	**41.05 (2.63)**	**.001**	**32.38 (2.95)**	**39.17 (3.25)**	**.001**
NECK LENGTH cm	**11.00 (1.19)**	**8.97 (1.25)**	**.001**	**9.907 (1.26)**	**8.25 (1.33)**	**.027**
AE1 cm^2	1.39 (0.48)	1.259 (0.56)	.397	1.37 (0.41)	1.11 (0.23)	.178
AE1M cm^2	**0.88 (0.43)**	**0.387 (0.34)**	**.001**	**0.97 (0.22)**	**0.102 (0.16)**	**.001**
AE2 cm^2	2.17 (0.67)	2.01 (0.62)	.392	1.92 (0.41)	1.62 (0.43)	.178
AE2M cm^2	**1.77 (0.59)**	**1.26 (0.53)**	**.002**	**1.65 (0.46)**	**0.94 (0.46)**	**.008**
AS1 cm^2	**1.40 (0.42)**	**1.13 (0.45)**	**.042**	**1.41 (0.27)**	**0.98 (0.32)**	**.008**
AS1M cm^2	**0.91 (0.28)**	**0.33 (0.27)**	**.001**	**1.03 (0.24)**	**0.11 (0.19)**	**.001**
AS2 cm^2	2.02 (0.66)	1.68 (0.54)	.050	1.77 (0.47)	1.87 (0.49)	.791
AS2M cm^2	**1.76 (0.56)**	**1.07 (0.51)**	**.001**	**1.55 (0.40)**	**0.89 (0.51)**	**.014**
TDE1 cm	1.43 (0.31)	1.25 (0.36)	.750	1.34 (0.24)	1.26 (0.23)	.519
TDE1M cm	**1.11 (0.41)**	**0.59 (0.45)**	**.001**	**1.13 (0.25)**	**0.23 (0.27)**	**.001**
TDE2 cm	1.64 (0.28)	1.59 (0.23)	.611	1.58 (0.24)	1.42 (0.20)	.235
TDE2M cm	**1.58 (0.29)**	1.27 (0.29)	**.001**	**1.52 (0.25)**	**1.16 (0.19)**	**.002**
TDS1 cm	**1.49 (0.27)**	**1.23 (0.29)**	**.003**	1.43 (0.23)	1.22 (0.17)	.066
TDS1M cm	**1.21 (0.29)**	**0.56 (0.39)**	**.001**	**1.18 (0.33)**	**0.17 (0.27)**	**.001**
TDS2 cm	**1.65 (0.28)**	**1.49 (0.24)**	**.029**	1.61 (0.20)	1.59 (0.31)	.791
TDS2M cm	**1.53 (0.24)**	**1.13 (0.35)**	**.001**	**1.45 (0.28)**	**1.05 (0.32)**	**.023**
LDE1 cm	1.16 (0.24)	1.18 (0.30)	.827	1.22 (0.20)	1.12 (0.19)	.381
LDE1M cm	**0.93 (0.32)**	**0.65 (0.44)**	**.021**	**1.06 (0.18)**	**0.30 (0.36)**	**.001**
LDE2 cm	1.62 (0.23)	1.52 (0.26)	.191	1.49 (1.49)	1.41 (0.21)	.569
LDE2M cm	1.35 (0.25)	1.23 (0.30)	.136	1.33 (0.23)	1.06 (0.45)	.154
LDS1 cm	1.11 (0.21)	1.11 (0.21)	.948	1.21 (0.12)	1.04 (0.33)	.080
LDS1M cm	**0.95 (0.21)**	**0.56 (0.40)**	**.001**	**1.07 (0.23)**	**0.27 (0.45)**	**.001**
LDS2 cm	1.49 (0.27)	1.37 (0.25)	.130	1.38 (0.18)	1.44 (0.18)	.519
LDS2M cm	**1.41 (0.29)**	**1.12 (0.37)**	**.008**	1.31 (0.20)	1.11 (0.40)	.302
CAE1 × 100%	**0.35 (0.21)**	**0.69 (0.27)**	**.001**	**0.28 (0.14)**	**0.92 (0.12)**	**.001**
CAE2 × 100%	**0.16 (0.12)**	**0.37 (0.20)**	**.001**	**0.14 (0.13)**	**0.44 (0.21)**	**.002**
CAS1 × 100%	**0.35 (0.11)**	**0.69 (0.26)**	**.001**	**0.27 (0.13)**	**0.90 (0.19)**	**.001**
CAS2 × 100%	**0.14 (0.13)**	**0.35 (0.26)**	**.001**	**0.12 (0.10)**	**0.53 (0.20)**	**.001**
CTDE1 × 100%	**0.21 (0.23)**	**0.54 (0.34)**	**.001**	**0.16 (0.10)**	**0.83 (0.21)**	**.001**
CTDE2 × 100%	**0.40 (0.10)**	**0.19 (0.16)**	**.001**	**0.04 (0.08)**	**0.18 (0.11)**	**.008**
CTDS1 × 100%	**0.21 (0.14)**	**0.56 (0.31)**	**.001**	**0.18 (0.16)**	**0.84 (0.24)**	**.001**
CTDS2 × 100%	**0.07 (0.10)**	**0.23 (0.21)**	**.001**	**0.80 (0.12)**	**0.47 (0.22)**	**.001**
CLDE1 × 100%	**0.15 (0.25)**	**0.46 (0.35)**	**.001**	**0.12 (0.12)**	**0.75 (0.29)**	**.001**
CLDE2 × 100%	0.12 (0.12)	0.18 (0.14)	.184	0.11 (0.11)	0.27 (0.23)	.055
CLDS1 × 100%	**0.13 (0.12)**	**0.49 (0.35)**	**.001**	**0.79 (0.37)**	**0.12 (0.15)**	**.003**
CLDS2 × 100%	0.06 (0.12)	0.18 (0.26)	.056	0.05 (0.12)	0.22 (0.26)	.112
TD/LD E1 ratio	**1.26 (0.28)**	**1.08 (0.29)**	**.040**	1.12 (0.23)	1.45 (0.25)	.302
TD/LD E2 ratio	1.00 (0.08)	1.05 (0.12)	.167	**1.06 (0.14)**	1.02 (0.17)	.424
TD/LD S1 ratio	**1.39 (0.31)**	**1.15 (0.32)**	**.014**	1.18 (0.18)	1.28 (0.44)	.677
TD/LD S2 ratio	1.12 (0.13)	1.09 (0.14)	.616	1.18 (0.15)	1.11 (0.17)	.424
AHI index/HR	**3.5 (1.51)**	**40.98 (23.34)**	**.001**	**3.19 (1.68)**	**31.25 (26.72)**	**.001**
Epworth	**4.09 (3.27)**	**11.60 (4.61)**	**.001**	3.68 (2.46)	7.00 (6.45)	.154
Age	**28.18 (9.43)**	**42.47 (10.96)**	**.001**	32.94 (10.23)	43.33 (13.00)	.117
Height m	**1.73 (0.58)**	**1.69 (0.05)**	**.042**	1.57 (0.05)	1.56 (0.08)	.641
Weight kg	**68.80 (2.21)**	**83.22 (14.69)**	**.001**	**55.70 (10.42)**	**72.12 (15.80)**	**.010**
BMI	**22.97 (3.68)**	**28.83 (5.01)**	**.001**	**22.62 (4.09)**	**29.57 (5.99)**	**.002**

Values are mean (SD).
Significant parameters and *P* values ($P < 0.05$) are in bold print.
OSA, obstructive sleep apnea; BMI, body mass index.

TABLE III.
ROC Values

Parameters/indices	Males			Females		
	ROC	95% CI	*p* Value	ROC	95% CI	*p* Value
Neck circumference cm	**0.8768**	**0.723–0.957**	**.001**	**0.9375**	**0.850–1.000**	**.002**
Neck length cm	**0.8747**	**0.746–0.970**	**.001**	**0.8073**	**0.562–1.000**	**.032**
AE1 cm^2	0.5747	0.418–0.732	.378	**0.7000**	**0.459–0.941**	**.161**
AE1M cm^2	**0.8220**	**0.696–0.950**	**.001**	**1.0000**	-	**.001**
AE2 cm^2	0.5724	0.404–0.740	.392	0.6944	0.451–0.938	.173
AE2M cm^2	**0.7564**	**0.631–0.882**	**.002**	**0.8611**	**0.681–1.000**	**.011**
AS1 cm^2	0.6735	0.524–0.823	.040	**0.8667**	**0.699–1.000**	**.010**
AS1M cm^2	**0.9284**	**0.861–0.996**	**.001**	**1.0000**	-	**.001**
AS2 cm^2	0.6554	0.504–0.807	.066	0.5389	0.256–0.822	.785
AS2M cm^2	**0.8183**	**0.706–0.993**	**.001**	**0.8444**	**0.620–1.000**	**.016**
TDE1 cm	0.6335	0.789–0.789	.115	0.6000	0.285–0.915	.484
TDE1M cm	**0.8167**	**0.691–0.943**	**.001**	**1.0000**	-	**.001**
TDE2 cm	0.5437	0.369–0.718	.605	0.6778	0.443–0.912	.213
TDE2M cm	**0.7722**	**0.642–0.902**	**.001**	**0.9056**	**0.776–1.000**	**.004**
TDS1 cm	**0.7459**	**0.611–0.880**	**.004**	**0.7667**	**0.555–0.978**	**.062**
TDS1M cm	**0.9208**	**0.850–0.991**	**.001**	**1.0000**	-	**.001**
TDS2 cm	0.6682	0.509–0.827	.047	0.5389	0.245–0.833	.785
TDS2M cm	**0.8401**	**0.733–0.947**	**.001**	**0.8222**	**0.595–1.000**	**.024**
LDE1 cm	0.5264	0.364–0.689	.755	0.6333	0.371–0.895	.350
LDE1M cm	0.6953	0.552–0.839	.021	**0.9778**	**0.922–1.000**	**.001**
LDE2 cm	0.6199	0.469–0.771	.157	0.5889	0.291–0.887	.533
LDE2M cm	0.6109	0.457–0.765	.190	**0.7056**	**0.424–0.987**	**.150**
LDS1 cm	0.4661	0.300–0.632	.688	**0.7556**	**0.459–1.000**	**.073**
LDS1M cm	**0.8175**	**0.705–0.930**	**.001**	**0.9389**	**0.817–1.000**	**.002**
LDS2 cm	0.6139	0.462–0.766	.179	0.6000	0.325–0.875	.484
LDS2M cm	0.6976	0.555–0.840	.020	0.6500	0.339–0.961	.293
CAE1 × 100%	**0.8304**	**0.719–0.957**	**.001**	**1.0000**	-	**.001**
CAE2 × 100%	**0.8054**	**0.653–0.901**	**.001**	**0.9111**	**0.786–1.000**	**.004**
CAS1 × 100%	**0.8800**	**0.798–0.975**	**.001**	**1.0000**	-	**.001**
CAS2 × 100%	**0.7966**	**0.712–0.928**	**.001**	**0.9778**	**0.923–1.000**	**.001**
CTDE1 × 100%	**0.7686**	**0.655–0.915**	**.001**	**1.0000**	-	**.001**
CTDE2 × 100%	**0.7879**	**0.704–0.937**	**.001**	**0.8667**	**0.688–1.000**	**.010**
CTDS1 × 100%	**0.8450**	**0.778–0.960**	**.001**	**1.0000**	-	**.001**
CTDS2 × 100%	**0.7879**	**0.684–0.924**	**.001**	**1.0000**	-	**.001**
CLDE1 × 100%	**0.7815**	**0.636–0.904**	**.001**	**0.9778**	**0.922–1.000**	**.001**
CLDE2 × 100%	0.5020	0.348–0.655	.986	**0.7778**	**0.485–1.000**	**.052**
CLDS1 × 100%	**0.8135**	**0.693–0.918**	**.001**	**0.9000**	**0.713–1.000**	**.005**
CLDS2 × 100%	0.6655	0.544–0.825	.029	**0.7333**	**0.454–1.000**	**.102**
TD/LD E1 ratio	0.6682	0.518–0.819	.047	0.6560	0.362–0.949	.276
TD/LD E2 ratio	0.6169	0.459–0.775	.167	0.6220	0.331–0.913	.392
TD/LD S1 ratio	**0.7059**	**0.561–0.851**	**.015**	0.567	0.215–0.919	.640
TD/LD S2 ratio	0.5588	0.385–0.733	.487	0.6220	0.329–0.915	.392
AHI index/HR	**0.9989**	**0.994–1.000**	**.001**	**0.9744**	**0.926–1.000**	**.001**
El worth	**0.8932**	**0.782–0.978**	**.001**	**0.7031**	**0.523–0.954**	**.094**
Age	**0.8430**	**0.662–0.934**	**.001**	**0.7280**	**0.451–1.000**	**.111**
Height m	0.6453	0.536–0.832	.030	0.5670	0.231–0.902	.640
Weight kg	**0.8034**	**0.627–0.908**	**.002**	**0.8560**	**0.691–1.000**	**.013**
BMI	**0.8658**	**0.717–0.961**	**.001**	**0.9000**	**0.766–1.000**	**.005**

Please note those M (Mueller) parameters and C (collapsibility)indices tend to have more significant *P* values *(P* < 0.05, in bold print)and higher values of predictability (ROC > 0.7, in bold print).

ROC, relative operating characteristics; CI, confidence interval; BMI, body mass index.

TABLE IV.
Endoscopic Clinical Predictors.

Male, AS1M (ROC = 0.9284)									
Cut-off cm^2	1.0533	0.9378	0.8611	0.7981	0.7404	0.6826	0.6197	0.5430	0.4275
PPV	75.00	82.61	84.09	86.05	87.50	92.11	94.12	96.88	96.30
NPV	100.00	90.00	83.33	84.62	75.00	77.78	68.18	66.67	55.17
Male, AS2M (ROC = 0.8183)									
Cut-off cm^2	2.5971	2.2773	2.0648	1.8906	1.7307	1.5708	1.3966	1.1840	0.8643
PPV	72.22	73.58	76.00	76.60	77.78	82.05	87.50	95.65	93.75
NPV	100.00	100.00	83.33	66.67	63.64	58.80	54.17	48.48	40.00
Female, TDE2M (ROC = 0.9056)									
Cut-off cm	1.3940	1.3382	1.3010	1.2706	1.2427	1.2147	1.1843	1.1471	1.0913
PPV	50.00	54.55	66.67	57.14	60.00	60.00	100.00	100.00	100.00
NPV	100.00	100.00	100.00	85.71	81.25	81.25	83.33	75.00	75.00

ROC, relative operating characteristics; PPV, positive predictive value; NPV, negative predictive value.

compared with indices obtained during resting/static measurement (ROC = 1) in female subjects. In the erect position, the ROC of measurements of resting areas was 0.9333, and the ROC of measurements of areas during Mueller's maneuver was 1. In the supine position, the ROC of measurements of resting areas was 1, and the ROC of measurements of areas during Mueller's maneuver was 1. In other words, the measurement of upper airway areas at the supine position has a slightly higher predictive value than at the erect position in both resting area and Mueller's maneuver measurements.

In addition, a further step was taken to pursue enhanced predictability with higher precision (higher PPV and NPV values) for retropalatal and retrolingual levels for both males and females by means of statistical modeling/formulas, which were derived from logistic regression. For males, the retropalatal predictive formula involved AS1 M, LDS1 M, and TDS1 M, and the ROC obtained was 0.9457, and, by setting the cut-off probability at 0.6, the PPV and NPV were 94.74% and 83.33%, respectively. For females, AS1 M had an ROC of 1, and thus no formula is required. For the retrolingual level, the predictive formula for males involved AS2 M, LDS2 M, and TDS2 M, and the ROC obtained was 0.8401, and, by setting the cut-off probability at 0.5, the PPV and NPV were 80.43% and 80%, respectively. No female retrolingual formula was required because a single predictor, TDE2 M, already had an excellent ROC of 0.9056, a PPV of 100%, and an NPV 0f 83.33%.

Apart from static and dynamic area measurements of the upper airway, the longitudinal and transverse diameters of the upper airway of all subjects at both the retropalatal and retrolingual levels, during quiet respiration and Mueller's maneuver in the both erect and supine positions, were also obtained. We compared the ratio of transverse/longitudinal (TD/LD) diameters between the groups of OSA patients and normal subjects in both erect and supine positions (Table II). In males, it was found that the configuration of upper airway at retropalatal level of normal subjects (mean TD/LD ratio was 1.2583 at E1, 1.3876 at S1) was more oval transversely than OSA patients (mean TD/LD ratio was 1.0829 at E1, 1.1514 at S1) (both $P < .05$) (Fig. 5). At the retrolingual level, the configurations of the upper airways of the normal subjects (mean TD/LD ratio was 1.0014 at E2, 1.1170 at S2) and OSA patients (mean TD/LD ratio was 1.0533 at E2, 1.0964 at S2) ($P > .05$) were similar. In females, it was found that the configuration of the upper airway at the retropalatal level of normal subjects (mean TD/LD ratio was 1.1224 at E1, 1.1791 at S1) was more oval longitudinally than OSA patients (mean TD/LD ratio was 1.4766 at E1, 1.2756 at S1) ($P > .05$). At the retrolingual level, the configurations of upper airway between the normal subjects (mean TD/LD ratio is 1.0640 at E2, 1.1770 at S2) and OSA patients (mean TD/LD ratio is 1.0223 at E2, 1.1072 at S2) were similar ($P > .05$).

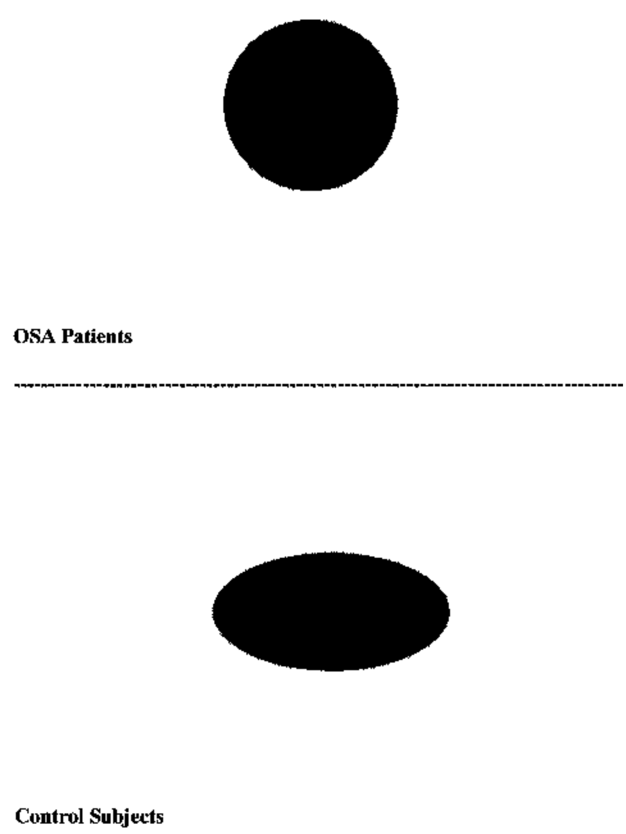


Fig. 5. Retropalatal airway configuration in males ($P < .05$). Diagrammatic representation (not to scale).

In this study, we also examined correlations of various parameters of upper airways with the severity of the OSA in terms of the AHI (Table V). For males, we analyzed all 36 parameters (absolute dimensions and derived collapsibility figures) to determine which parameters had good linear correlation with severity of OSA (indicated by severity of AHI).

Using bivariate linear correlation, we discovered that two parameters have good correlation with the severity of OSA in terms of AHI. The two parameters are AS1 M and CAS1 (Fig. 6). Each of these two parameters has an R (correlation coefficient) value of greater than 0.6 and a *P* value less than .05. Earlier in this study, AS1 M was observed to be an excellent marker for predicting OSA at the retropalatal level. Coupled with its good correlation with the severity of AHI, it can be concluded that AS1 M is an outstanding marker for the presence and severity of OSA disease at the retropalatal level.

From Table V, in general, collapsibility parameters have positive R values, meaning that the higher the collapsibility parameter, the higher the AHI. On the other hand, absolute dimensions that have negative R values (correlations) indicate that the larger the airway dimensions, the smaller the AHI indices. It was also observed that, for absolute dimensions, those performed during Mueller's maneuver have a stronger correlation with AHI severity than those performed at the resting phase (quite respiration). We did not perform the correlation study on the female group because the size of sample was smaller, with much less significant results.

TABLE V.
Correlations (males).

	AHI	*P* Value
AE1	−.190	.161
AE1M	**−.422**	**.001**
AE2	−.035	.799
AE2M	−.247	.067
AS1	−.237	.078
AS1M	**−.639**	**<.001**
AS2	−.148	.275
AS2M	−.243	.071
TDE1	**−.354**	**.007**
TDE1M	**−.492**	**<.001**
TDE2	−.015	.912
TDE2M	**−.387**	**.003**
TDS1	**−.431**	**.001**
TDS1M	**−.540**	**<.001**
TDS2	−.140	.304
TDS2M	−.240	.075
LDE1	−.025	.852
LDE1M	**−.338**	**.011**
LDE2	−.028	.840
LDE2M	−.066	.627
LDS1	−.095	.488
LDS1M	**−.476**	**<.001**
LDS2	−.113	.407
LDS2M	−.056	.682
CAE1	**.483**	**<.001**
CAE2	**.360**	**.004**
CAS1	**.611**	**<.001**
CAS2	.178	.169
CTDE1	**.475**	**<.001**
CTDE2	**.437**	**<.001**
CTDS1	**.453**	**<.001**
CTDS2	.184	.155
CLDE1	**.462**	**<.001**
CLDE2	.028	.832
CLDS1	**.557**	**<.001**
CLDS2	.050	.704
td_ld_e1	**−.353**	**.008**
td_ld_e2	−.016	.905
td_ld_s1	**−.405**	**.002**
td_ld_s2	−.003	.981

AHI, apnea-hypopnea index.

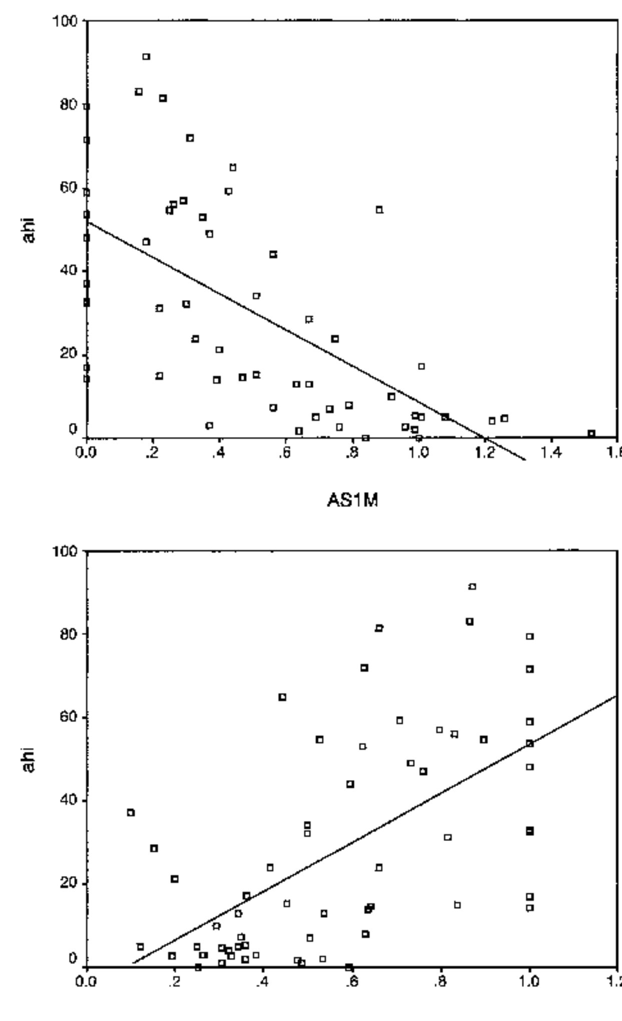


Fig. 6. Correlations between severity of obstructive sleep apnea (OSA) (apnea-hypopnea index) and AS1M (retropalatal area measured in the supine position during Mueller's maneuver) and CAS1 (collapsibility of retropalatal area in the supine position) in OSA males.

DISCUSSION

There have been many attempts to derive easily obtainable predictors for OSA, which are complementary to PSG in evaluation of patients suspected of OSA. These predictors can be divided into clinical or radiologic (e.g., cephalometric). Clinical predictors can be further subdivided into simple physical examination or endoscopic examination. Friedman et al.,[2] presented the Friedman score as a tool to help identify patients who should have full sleep evaluation. Their results validated the usefulness of the Friedman score in identifying patients with severe OSA and those who might benefit from uvulopalatopharyngoplasty. However, the score uses subjective grading of the various parameters and may be prone to interobserver variability. The modified Malampatti grade and tonsil size are both indirect measures to estimate the extent of oropharyngeal and hypopharyngeal narrowing from bulky tongues and tonsils. It would be desirable to be able to directly assess and quantitatively measure retropalatal morphology .

In this study, absolute dimensions (cross-sectional area, transverse diameter, and longitudinal diameter) of the upper airway in both males and females during quiet respiration were not found to predict OSA very well. Mueller's studies, on the other hand, using dimensions obtained during Mueller's maneuver and calculated indices such as collapsibility of the upper airway in both males and females, were proven to be strong (statistically and clinically significant) predictors of OSA. It was concluded, on the basis of this study, that Mueller's measurements were more useful than static ones in predicting OSA.

The Mueller's maneuver as an aid in upper airway assessment has also been validated in various studies by Sher et al.,[7] Ritter et al.,[8] and other investigators.[9–11] Terris et al.[9] explored the reliability of the Mueller's maneuver by using a 5-point scale scored by different independent examiners to achieve an objective and reproducible upper airway assessment and found that the severity of sleep-disordered breathing based on AHI is correlated with Mueller's maneuver. Most of these investigators graded their findings on the basis of a visual estimation of the ratio of collapsibility in terms of percentage decrease in retropalatal diameter. These take into account only one dimension, which contributes to the retropalatal area. It was shown in this study that the direction of collapse and the final shape of the retropalatal space might not be constant. Thus, collapsibility and absolute area measurements provide a better, more objective approach than any one dimension estimated visually. It was realized that parameters/indices obtained in the supine position have better predictive values for OSA than those obtained in the erect position. It may thus be sufficient to perform upper airway assessment and obtain measurement only in the supine position. Among the factors that were found to have predictive value for OSA, for the purpose of simplicity and ease of usage, two sets of anatomic values with excellent predictive value for both males and females were selected. For males, an AS1 M of less than 0.7981 cm^2 for the retropalatal level and an AS2 M of less than 2.0648 cm^2 for the retrolingual level were selected. AS1 M and CAS1 were also found to have good correlations with severity of OSA. For females, an AS1 M of less than 0.522cm^2 for the retropalatal level and a TDE2 M of less than 1.1843 cm for the retrolingual level were selected. The logistic regression-derived formulas mentioned above would certainly help to raise the predictability for OSA, thereby assisting surgeons in their clinical assessment of patients, especially when surgical intervention is the chosen treatment option.

In practice, quantitative videoendoscopy can be performed in the outpatient setting and the measurements easily obtained at the same clinic visit. The predictors detailed above provide surgeons with information regarding the probability that the patient has OSA and allow surgeons to plan treatment accordingly. Airway measurements with this quantitative videoendoscopy during sleep would be more physiologic and realistic in nature, and, therefore, it should be considered in our future studies. On the basis of this study alone, there may not be sufficient information to recommend a specific surgical procedure. We can surmise that patients who meet retropalatal criteria for OSA would benefit from palatal surgery and similarly for retrolingual criteria. Earlier studies into the efficacy of various types of surgery for OSA were based largely on subjective observations. Quantitative videoendoscopy would also allow surgeons to objectively assess postoperative changes in upper airway morphology and dynamics to rationalize and perhaps modify surgical procedures in the future.

CONCLUSION

This study provides sex and anatomic-site specific OSA predictors and formulas, assisting surgeons to accurately define the location of upper airway obstruction and address it with appropriate surgery.

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