10th Yahya Cohen Memorial Lecture: Clinical Predictors in Obstructive Sleep Apnoea Patients with Computer-assisted Quantitative Videoendoscopic Upper Airway Analysis

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Abstract

Aim: To identify the clinical predictors and assist surgeons in their clinical management of obstructive sleep apnoea (OSA) – a prospective study with a new approach to analyse the static and dynamic upper airway morphology between patients with OSA and normal subjects. To introduce a new method of assessment for surgical outcome. Materials and Methods: 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 (apnoea-hypopnoea index <5). Absolute cross-sectional areas, transverse and longitudinal diameters at the retro-palatal and retro-lingual levels were measured during end of quiet respiration and during Mueller's manoeuvre in the erect and supine positions, allowing us to study static and dynamic morphology (collapsibility) of the upper airway. We analysed 3744 parameters. Results: In males, retro-palatal and retro-lingual areas during Mueller's manoeuvre in the supine position of 0.7981 cm^2 [receiver operating characteristics (ROC) = 0.9284, positive predictive value (PPV) = 86.05%, negative predictive value (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. Retro-palatal area measured in the supine position during Mueller's manoeuvre (AS1M) and collapsibility of retro-palatal area in the supine position calculated (CAS1) were found to have significant correlations with severity of OSA. In females, areas measured during Mueller's manoeuvre in the supine position of 0.522 cm^2 at retro-palatal level (ROC = 1, 100% PPV and NPV) and transverse diameter at retro-lingual level during erect Mueller's manoeuvre of 1.1843 cm (ROC = 0.9056, PPV = 100%, NPV = 83.33%) were found to be predictive. All measurements at the retro-palatal level and in the supine position had higher predictability. Area measurements obtained during Muller's manoeuvre were more predictive (ROC >0.9910) than resting measurements (ROC >0.8371). Several gender and anatomical-site specific formulas with excellent predictability (ROC close or equal to 1) were also devised. Examples of surgical outcome assessment were introduced. 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 gender and anatomical-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.

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Key words: Mueller's study, OSA predictors

Introduction

Obstructive sleep apnoea (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), Malampatti score[2] and tonsil size to lateral cephalometric measurements[3,4] and nasopharyngoscopic

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assessment with or without Mueller's manoeuvre. Nasopharyngoscopy is a widely available technique commonly performed by otolaryngologists to evaluate the upper airway. This technique is easily performed in 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 manoeuvre is an ideal modality to examine dynamic changes in upper airway calibre, it can be used to determine the extent of retro-palatal or retro-glossal obstruction. The Mueller's manoeuvre is thought to simulate the upper airway collapse that occurs during apnoea 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 manoeuvre may not be the same as during an apnoeic 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 manoeuvre. The methods of assessment in these early studies were all non-quantitative, 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 characterise the static and dynamic morphology of the subjects' upper airway and to derive reliable indicators to predict OSA.

Materials and Methods

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 (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 [apnoea-hypopnoea index (AHI) <5] and lowest oxygen saturation >90%. Those control subjects recruited with sleep study of AHI ≥5 and with a lowest oxygen saturation of <90% were excluded from the control group.

Subsequently, PSG data and videoendoscopic analysis results were collated and added to the database before analysis.

Polysomnography

Polysomnography was performed over one night on all subjects. It included electroencephalogram (EEG, C3/A2, C4/A1, O2/A1), submental electromyogram (EMG), anterior tibialis EMG, electrocardiogram, thoraco-abdominal motion, oronasal airflow (expired CO2), and arterial oxygen saturation with pulse oximetry. The studies were scored manually, and the total AHI was calculated for that night. Obstructive apnoea was defined as the cessation of airflow for at least 10 seconds accompanied by ongoing respiratory efforts. Hypopnoea 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), 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/practise Mueller's manoeuvre until they were comfortable before the procedure started. The examination began with introduction of lubricated nasopharyngoscope and examined the entire upper airway 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 (retro-palatal or retro-lingual levels). Once the desired level was reached with the calibrator, the surgeon performing the procedure would take note of the length of the calibrator and the scope was inserted. In addition, anatomical landmarks were also used to guide the positioning of the calibrator at these two levels. The uvula was used as the landmark for the retro-palatal level and the tip of the epiglottis was used as the anatomical landmark for the retro-lingual level. The purpose of these measures was to ensure the consistent positions of calibrator in airway measurements during both resting phase and Mueller's manoeuvre.

A video record of the entire examination was made, which included quiet respiration and Mueller's manoeuvre, 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 Inc, California, USA) and digital imaging software (JasCapture Version Shareware 2.0, JASC Inc, Minnesota, USA) 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 upper airway), was employed. The actual dimensions were obtained by comparing the calibrator (5 mm) with these videoendoscopic images. Measurements were taken during end of quiet respiration, during Mueller's manoeuvre, and in erect and supine positions at two levels, namely the retro-palatal and retro-lingual levels (8 images per patient 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 manoeuvre with the original measurement obtained during quiet respiration and expressed in terms of percentages. All measurements and calculated information (3744 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; 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 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 analysed 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 retro-palatal and retro-lingual levels. Two videoendoscopic images per patient, with a total of 90 images were compared with MRI scans. Once these 2 images were validated by MRI scans, we could assume (extrapolate) the remaining videoendoscopic images (Mueller's manoeuvre, 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 retro-palatal level and 92.34% at the retro-lingual level. These results indicate that this method of measurement gives consistently accurate upper airway measurement results.

Data Analysis

Statistically significant (P <0.05) parameters and indices between OSA and normal subjects within gender were determined using independent samples *t*-test and Mann-Whitney U test. Receiver operating characteristic (ROC) curves were used to derive the predictive values of various parameters for OSA. Logistic regression was used to derive these predictive modelling/formulas.

Results

There were 49 (43 males, 6 females) patients with OSA and 39 (22 males, 17 females) control subjects (PSG AHI <5). Table 1 shows the nomenclature for the naming convention of the variables of this study. For example, AE1M means the cross-sectional area measured at retro-palatal level at erect position during the Mueller's manoeuvre. Without the letter M indicates the measurement obtained during quiet respiration. Table 2 gives the comparison of descriptive statistics between OSA patients and controls within gender; significant differences (P <0.05) between the 2 groups are in bold. For both genders, neck circumference, neck length, AE1M, AE2M, AS1, AS1M, AS2M, TDE1M, TDE2M, TDS1M, TDS2M, LDE1M, LDS1M, CAE1, CAE2, CAS1, CAS2, CTDE1, CTDE2, CTDS1, CTDS2, CLDE1, CLDS1, weight and BMI were significantly different between controls and OSA patients. Epworth, age, height, TDS1, TDS2, LDS2M, TD/LD E1 and TD/LDS1 were also significantly different for the males only.

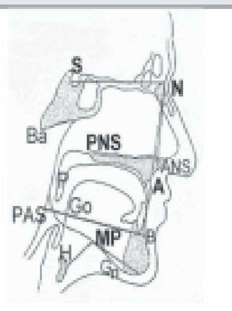
ROC curves were used to determine the parameters that were good predictors (ROC >0.7, maximum ROC = 1) of OSA (Table 3) (ROC >0.7 are in bold). For both genders, age, weight, Epworth score, BMI, neck circumference and length, AE1M, AE2M, AS1M, AS2M, TDE1M, TDE2M, TDS1, TDS1M, TDS2M, LDS1M, CAE1, CAE2, CAS1, CAS2, CTDE1, CTDE2, CTDS1, CTDS2, CLDE1 and CLDS1 gave ROC >0.7. For female patients, AE1, AS1, LDE1M, LDE2M, LDS1, CLDE2 and CLDS2 also gave ROC >0.7; whereas for males, only TD/LD S1 gave ROC >0.7.

For each of the parameters that was found to be good

Patient HRN:		Name:
~~C~~ / D	Pre / ~~Post~~	Visit Date: 29/12/2000

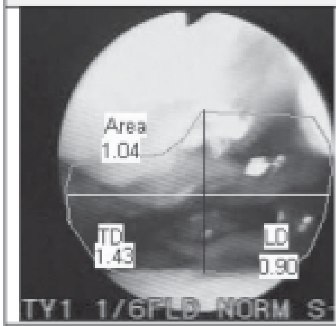
DOB: 03/07/1961
Age: 40 Sex: M
Race: Chinese
Wt: 95 kg Ht: 1.7 m
Neck Circum: 48 cm
Neck Length: 8 cm
BMI: 32.87
AHI: 68 /hr
AI: 28 /hr

Lowest O_2 sat: 60 %
MRI: Y/~~N~~ (02/01/2001)
Dietician: Y/~~N~~
CPAP: Y/~~N~~ On Trial
Epworth : 20
Nasal:
Septum: Deviated
I-turbinate: Normal

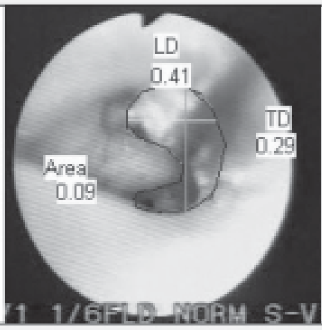


C-metry	Erect	Supine
SNA:	80 °	80 °
SNB:	78 °	78 °
NSBa:	140 °	140 °
N-ANS:	45 mm	45 mm
ANS-Gn:	72 mm	72 mm
PAS:	14 mm	10 mm
MP-H:	24 mm	28 mm
PNS-P:	35 mm	40 mm
R-Pa:	9 mm	4 mm
Pa:	12 mm	9 mm

Erect Level One



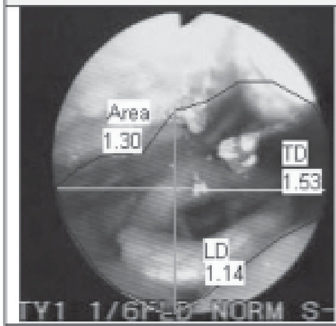
Erect Level One Muller



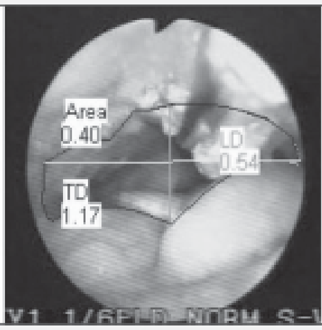
History

40 years old Chinese male, Taxi driver, C/o of increasing daytime sleepiness over last 3 years, and severely affects his job and marriage life.

Erect Level Two



Erect Level Two Muller



Collapsibility (%)

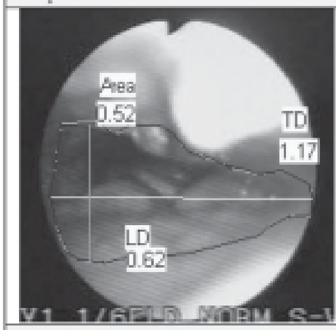
Erect level 1 (Uvula)

Surface Area	: **91.35** %
Transverse Diameter	: **79.72** %
Longitudinal Diameter	: **54.44** %

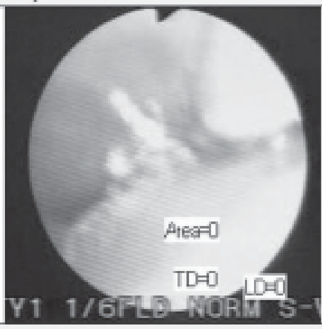
Erect level 2 (Epiglottis)

Surface Area	: **69.23** %
Transverse Diameter	: **23.53** %
Longitudinal Diameter	: **52.63** %

Supine Level One



Supine Level One Muller



Collapsibility (%)

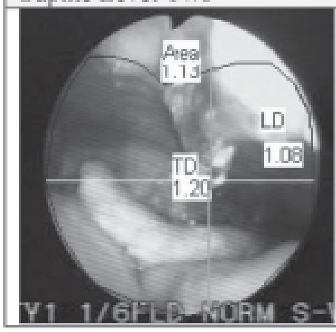
Supine level 1 (Uvula)

Surface Area	: **100.00** %
Transverse Diameter	: **100.00** %
Longitudinal Diameter	: **100.00** %

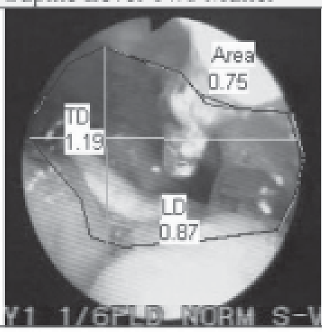
Supine level 2 (Epiglottis)

Surface Area	: **33.63** %
Transverse Diameter	: **0.83** %
Longitudinal Diameter	: **19.44**%

Supine Level Two



Supine Level Two Muller



Comment:

On weight reduction program, diet control, behaviour counseling, and CPAP trial.

To be reviewed in 2 months.

Fig. 1. Clinical summary and measurement data.

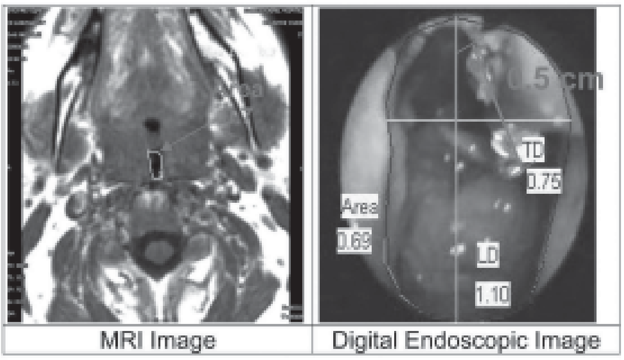
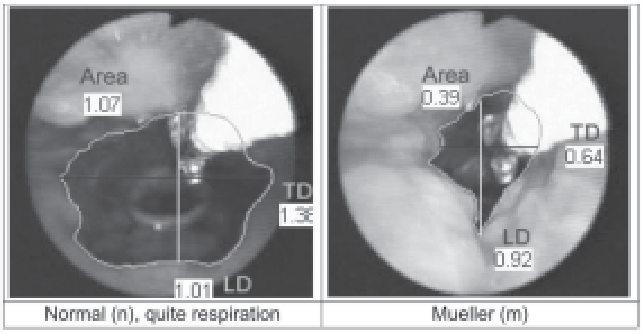


Fig. 2. Measurements validation: comparing the area measurement between the upper airway magnetic resonance image and digital endoscopic image at the identical level of upper airway.



Example of Calculation of Collapsibility

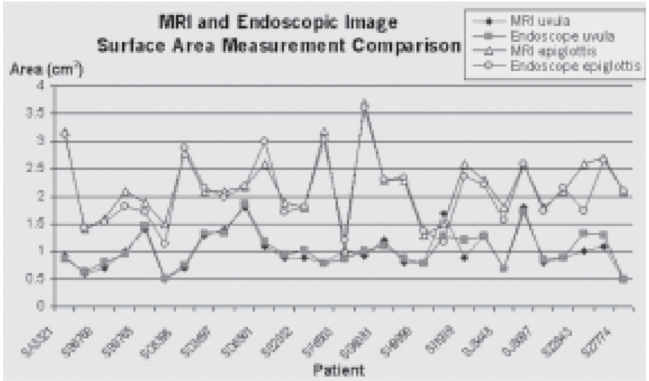
- Area collapsibility = $\frac{\text{Area(n)} - \text{Area(m)}}{\text{Area(n)}}$

  $= \frac{1.07 - 0.39}{1.07}$

  = 63.56 %

- TD and LD collapsibilities are similarly calculated

Fig. 3. Example of calculation of collapsibility.



Difference (cm²)	Level 1	Level 2
<= 0.5	100 %	95.6 %
<= 0.4	97.8 %	91.1 %
<= 0.3	93.3 %	77.8 %

Surface area measurements of magnetic resonance imaging (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 (DI) were compared with the MRI measurements in each pair. The above chart shows the close proximity between 2 methods of measurements.

Fig. 4. Accuracy of computer-assisted endoscopic measurement.

Table 1. Nomenclature

A	area
TD	transverse diameter
LD	longitudinal diameter
E	erect position
S	supine position
Level 1	retro-palatal level
Level 2	retro-lingual level
M	Mueller manoeuvre
C	collapsibility
OSA	obstructive sleep apnoea
ROC	receiver operating characteristics
CAM	computer-assisted-quantitative videoendoscopic analysis

predictors for OSA, a cut-off value could be calculated to provide an indication of the likelihood of OSA. In order 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. For males, AS1M at <0.7981 cm^2 was chosen to be the single predictor for OSA at the retro-palatal level as it has the highest ROC (0.9284) with excellent positive predictive value (PPV) of 86.05% and negative predictive value (NPV) of 84.62% (Table 3). For the retro-lingual level, AS2M <2.0648 cm^2 was chosen as it has the highest ROC value (0.8183) with PPV of 76% and NPV of 83.33% (Table 4).

In males, indices obtained during Mueller's manoeuvre and thus calculated collapsibility were more predictive (ROC >0.9910) than resting/static area measurements (ROC >0.8371). This study compared the predictive value of anatomical parameters (both at rest and during Mueller's manoeuvre) 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 manoeuvre 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 manoeuvre was 0.9759. 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 manoeuvre.

For females, there were many parameters and indices with very high ROC, PPV and NPV values. But, again, in order to simplify the large number of significant parameters,

Table 2. Comparison of Descriptive Obstructive Sleep Apnoea (OSA) Data Between OSA Patients and Controls Within Gender

	Males			Females		
Parameters	Control	OSA	*P*	Control	OSA	*P*
Neck circumference (cm)	**37.18 (2.15)**	**41.05 (2.63)**	**0.001**	**32.38 (2.95)**	**39.17 (3.25)**	**0.001**
Neck length (cm)	**11.00 (1.19)**	**8.97 (1.25)**	**0.001**	**9.907 (1.26)**	**8.25 (1.33)**	**0.027**
AE1 (cm^2)	1.39 (0.48)	1.259 (0.56)	0.397	1.37 (0.41)	1.11 (0.23)	0.178
AE1M (cm^2)	**0.88 (0.43)**	**0.387 (0.34)**	**0.001**	**0.97 (0.22)**	**0.102 (0.16)**	**0.001**
AE2 (cm^2)	2.17 (0.67)	2.01 (0.62)	0.392	1.92 (0.41)	1.62 (0.43)	0.178
AE2M (cm^2)	**1.77 (0.59)**	**1.26 (0.53)**	**0.002**	**1.65 (0.46)**	**0.94 (0.46)**	**0.008**
AS1 (cm^2)	**1.40 (0.42)**	**1.13 (0.45)**	**0.042**	**1.41 (0.27)**	**0.98 (0.32)**	**0.008**
AS1M (cm^2)	**0.91 (0.28)**	**0.33 (0.27)**	**0.001**	**1.03 (0.24)**	**0.11 (0.19)**	**0.001**
AS2 (cm^2)	2.02 (0.66)	1.68 (0.54)	0.050	1.77 (0.47)	1.87 (0.49)	0.791
AS2M (cm^2)	**1.76 (0.56)**	**1.07 (0.51)**	**0.001**	**1.55 (0.40)**	**0.89 (0.51)**	**0.014**
TDE1 (cm)	1.43 (0.31)	1.25 (0.36)	0.750	1.34 (0.24)	1.26 (0.23)	0.519
TDE1M (cm)	**1.11 (0.41)**	**0.59 (0.45)**	**0.001**	**1.13 (0.25)**	**0.23 (0.27)**	**0.001**
TDE2 (cm)	1.64 (0.28)	1.59 (0.23)	0.611	1.58 (0.24)	1.42 (0.20)	0.235
TDE2M (cm)	**1.58 (0.29)**	**1.27 (0.29)**	**0.001**	**1.52 (0.25)**	**1.16 (0.19)**	**0.002**
TDS1 (cm)	**1.49 (0.27)**	**1.23 (0.29)**	**0.003**	1.43 (0.23)	1.22 (0.17)	0.066
TDS1M (cm)	**1.21 (0.29)**	**0.56 (0.39)**	**0.001**	**1.18 (0.33)**	**0.17 (0.27)**	**0.001**
TDS2 (cm)	**1.65 (0.28)**	**1.49 (0.24)**	**0.029**	1.61 (0.20)	1.59 (0.31)	0.791
TDS2M (cm)	**1.53 (0.24)**	**1.13 (0.35)**	**0.001**	**1.45 (0.28)**	**1.05 (0.32)**	**0.023**
LDE1 (cm)	1.16 (0.24)	1.18 (0.30)	0.827	1.22 (0.20)	1.12 (0.19)	0.381
LDE1M (cm)	**0.93 (0.32)**	**0.65 (0.44)**	**0.021**	**1.06 (0.18)**	**0.30 (0.36)**	**0.001**
LDE2 (cm)	1.62 (0.23)	1.52 (0.26)	0.191	1.49 (1.49)	1.41 (0.21)	0.569
LDE2M (cm)	1.35 (0.25)	1.23 (0.30)	0.136	1.33 (0.23)	1.06 (0.45)	0.154
LDS1 (cm)	1.11 (0.21)	1.11 (0.21)	0.948	1.21 (0.12)	1.04 (0.33)	0.080
LDS1M (cm)	**0.95 (0.21)**	**0.56 (0.40)**	**0.001**	**1.07 (0.23)**	**0.27 (0.45)**	**0.001**
LDS2 (cm)	1.49 (0.27)	1.37 (0.25)	0.130	1.38 (0.18)	1.44 (0.18)	0.519
LDS2M (cm)	**1.41 (0.29)**	**1.12 (0.37)**	**0.008**	1.31 (0.20)	1.11 (0.40)	0.302
CAE1 x 100%	**0.35 (0.21)**	**0.69 (0.27)**	**0.001**	**0.28 (0.14)**	**0.92 (0.12)**	**0.001**
CAE2 x 100%	**0.16 (0.12)**	**0.37 (0.20)**	**0.001**	**0.14 (0.13)**	**0.44 (0.21)**	**0.002**
CAS1 x 100%	**0.35 (0.11)**	**0.69 (0.26)**	**0.001**	**0.27 (0.13)**	**0.90 (0.19)**	**0.001**
CAS2 x 100%	**0.14 (0.13)**	**0.35 (0.26)**	**0.001**	**0.12 (0.10)**	**0.53 (0.20)**	**0.001**
CTDE1 x 100%	**0.21 (0.23)**	**0.54 (0.34)**	**0.001**	**0.16 (0.10)**	**0.83 (0.21)**	**0.001**
CTDE2 x 100%	**0.40 (0.10)**	**0.19 (0.16)**	**0.001**	**0.04 (0.08)**	**0.18 (0.11)**	**0.008**
CTDS1 x 100%	**0.21 (0.14)**	**0.56 (0.31)**	**0.001**	**0.18 (0.16)**	**0.84 (0.24)**	**0.001**
CTDS2 x 100%	**0.07 (0.10)**	**0.23 (0.21)**	**0.001**	**0.80 (0.12)**	**0.47 (0.22)**	**0.001**
CLDE1 x 100%	**0.15 (0.25)**	**0.46 (0.35)**	**0.001**	**0.12 (0.12)**	**0.75 (0.29)**	**0.001**
CLDE2 x 100%	0.12 (0.12)	0.18 (0.14)	0.184	0.11 (0.11)	0.27 (0.23)	0.055
CLDS1 x 100%	**0.13 (0.12)**	**0.49 (0.35)**	**0.001**	**0.79 (0.37)**	**0.12 (0.15)**	**0.003**
CLDS2 x 100%	0.06 (0.12)	0.18 (0.26)	0.056	0.05 (0.12)	0.22 (0.26)	0.112
TD/LD E1 ratio	**1.26 (0.28)**	**1.08 (0.29)**	**0.040**	1.12 (0.23)	1.45 (0.25)	0.302
TD/LD E2 ratio	1.00 (0.08)	1.05 (0.12)	0.167	1.06 (0.14)	1.02 (0.17)	0.424
TD/LD S1 ratio	**1.39 (0.31)**	**1.15 (0.32)**	**0.014**	1.18 (0.18)	1.28 (0.44)	0.677
TD/LD S2 ratio	1.12 (0.13)	1.09 (0.14)	0.616	1.18 (0.15)	1.11 (0.17)	0.424
AHI index/hour	**3.5 (1.51)**	**40.98 (23.34)**	**0.001**	**3.19 (1.68)**	**31.25 (26.72)**	**0.001**
Epworth	**4.09 (3.27)**	**11.60 (4.61)**	**0.001**	3.68 (2.46)	7.00 (6.45)	0.154
Age	**28.18 (9.43)**	**42.47 (10.96)**	**0.001**	32.94 (10.23)	43.33 (13.00)	0.117
Height (m)	**1.73 (0.58)**	**1.69 (0.05)**	**0.042**	1.57 (0.05)	1.56 (0.08)	0.641
Weight (kg)	**68.80 (2.21)**	**83.22 (14.69)**	**0.001**	**55.70 (10.42)**	**72.12 (15.80)**	**0.010**
Body mass index	**22.97 (3.68)**	**28.83 (5.01)**	**0.001**	**22.62 (4.09)**	**29.57 (5.99)**	**0.002**

AHI: apnoea-hypopnoea index

Values are mean [standard deviation (SD)]; significant parameters and *P* values ($P < 0.05$) are in bold print.

AS1M <0.522 cm^2 at the retro-palatal level gave ROC = 1 and 100% PPV and NPV was selected. For the retro-lingual level, TDE2M <1.1843 cm with ROC = 0.9056 and PPV of 100% and NPV of 83.33% was selected (Table 4).

In contrast to the results for male subjects, the indices obtained during Mueller's manoeuvre and hence collapsibility were equally predictive (ROC = 1) when compared with indices obtained during resting/static

Table 3. Comparison of Receiver Operating Characteristics (ROC) Values Within Gender

	Males			Females		
Parameters/Indices	ROC	95% CI	*P*	ROC	95% CI	*P*
Neck circumference (cm)	**0.8768**	**0.723-0.957**	**0.001**	**0.9375**	**0.850-1.000**	**0.002**
Neck length (cm)	**0.8747**	**0.746-0.970**	**0.001**	**0.8073**	**0.562-1.000**	**0.032**
AE1 (cm^2)	0.5747	0.418-0.732	0.378	**0.7000**	**0.459-0.941**	**0.161**
AE1M (cm^2)	**0.8220**	**0.696-0.950**	**0.001**	**1.0000**	**-**	**0.001**
AE2 (cm^2)	0.5724	0.404-0.740	0.392	0.6944	0.451-0.938	0.173
AE2M (cm^2)	**0.7564**	**0.631-0.882**	**0.002**	**0.8611**	**0.681-1.000**	**0.011**
AS1 (cm^2)	0.6735	0.524-0.823	0.040	**0.8667**	**0.699-1.000**	**0.010**
AS1M (cm^2)	**0.9284**	**0.861-0.996**	**0.001**	**1.0000**	**-**	**0.001**
AS2 (cm^2)	0.6554	0.504-0.807	0.066	0.5389	0.256-0.822	0.785
AS2M (cm^2)	**0.8183**	**0.706-0.993**	**0.001**	**0.8444**	**0.620-1.000**	**0.016**
TDE1 (cm)	0.6335	0.789-0.789	0.115	0.6000	0.285-0.915	0.484
TDE1M (cm)	**0.8167**	**0.691-0.943**	**0.001**	**1.0000**	**-**	**0.001**
TDE2 (cm)	0.5437	0.369-0.718	0.605	0.6778	0.443-0.912	0.213
TDE2M (cm)	**0.7722**	**0.642-0.902**	**0.001**	**0.9056**	**0.776-1.000**	**0.004**
TDS1 (cm)	**0.7459**	**0.611-0.880**	**0.004**	**0.7667**	**0.555-0.978**	**0.062**
TDS1M (cm)	**0.9208**	**0.850-0.991**	**0.001**	**1.0000**	**-**	**0.001**
TDS2 (cm)	0.6682	0.509-0.827	0.047	0.5389	0.245-0.833	0.785
TDS2M (cm)	**0.8401**	**0.733-0.947**	**0.001**	**0.8222**	**0.595-1.000**	**0.024**
LDE1 (cm)	0.5264	0.364-0.689	0.755	0.6333	0.371-0.895	0.350
LDE1M (cm)	0.6953	0.552-0.839	0.021	**0.9778**	**0.922-1.000**	**0.001**
LDE2 (cm)	0.6199	0.469-0.771	0.157	0.5889	0.291-0.887	0.533
LDE2M (cm)	0.6109	0.457-0.765	0.190	**0.7056**	**0.424-0.987**	**0.150**
LDS1 (cm)	0.4661	0.300-0.632	0.688	**0.7556**	**0.459-1.000**	**0.073**
LDS1M (cm)	**0.8175**	**0.705-0.930**	**0.001**	**0.9389**	**0.817-1.000**	**0.002**
LDS2 (cm)	0.6139	0.462-0.766	0.179	0.6000	0.325-0.875	0.484
LDS2M (cm)	0.6976	0.555-0.840	0.020	0.6500	0.339-0.961	0.293
CAE1 x 100%	**0.8304**	**0.719-0.957**	**0.001**	**1.0000**	**-**	**0.001**
CAE2 x 100%	**0.8054**	**0.653-0.901**	**0.001**	**0.9111**	**0.786-1.000**	**0.004**
CAS1 x 100%	**0.8800**	**0.798-0.975**	**0.001**	**1.0000**	**-**	**0.001**
CAS2 x 100%	**0.7966**	**0.712-0.928**	**0.001**	**0.9778**	**0.923-1.000**	**0.001**
CTDE1 x 100%	**0.7686**	**0.655-0.915**	**0.001**	**1.0000**	**-**	**0.001**
CTDE2 x 100%	**0.7879**	**0.704-0.937**	**0.001**	**0.8667**	**0.688-1.000**	**0.010**
CTDS1 x 100%	**0.8450**	**0.778-0.960**	**0.001**	**1.0000**	**-**	**0.001**
CTDS2 x 100%	**0.7879**	**0.684-0.924**	**0.001**	**1.0000**	**-**	**0.001**
CLDE1 x 100%	**0.7815**	**0.636-0.904**	**0.001**	**0.9778**	**0.922-1.000**	**0.001**
CLDE2 x 100%	0.5020	0.348-0.655	0.986	**0.7778**	**0.485-1.000**	**0.052**
CLDS1 x 100%	**0.8135**	**0.693-0.918**	**0.001**	**0.9000**	**0.713-1.000**	**0.005**
CLDS2 x 100%	0.6655	0.544-0.825	0.029	**0.7333**	**0.454-1.000**	**0.102**
TD/LD E1 ratio	0.6682	0.518-0.819	0.047	0.6560	0.362-0.949	0.276
TD/LD E2 ratio	0.6169	0.459-0.775	0.167	0.6220	0.331-0.913	0.392
TD/LD S1 ratio	**0.7059**	**0.561-0.851**	**0.015**	0.5670	0.215-0.919	0.640
TD/LD S2 ratio	0.5588	0.385-0.733	0.487	0.6220	0.329-0.915	0.392
AHI index/hour	**0.9989**	**0.994-1.000**	**0.001**	**0.9744**	**0.926-1.000**	**0.001**
Epworth	**0.8932**	**0.782-0.978**	**0.001**	**0.7031**	**0.523-0.954**	**0.094**
Age	**0.8430**	**0.662-0.934**	**0.001**	**0.7280**	**0.451-1.000**	**0.111**
Height (m)	0.6453	0.536-0.832	0.030	0.5670	0.231-0.902	0.640
Weight (kg)	**0.8034**	**0.627-0.908**	**0.002**	**0.8560**	**0.691-1.000**	**0.013**
Body mass index	**0.8658**	**0.717-0.961**	**0.001**	**0.9000**	**0.766-1.000**	**0.005**

AHI: apnoea-hypopnoea index

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).

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 manoeuvre 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 manoeuvre was 1. The measurement of upper airway areas at the supine position has a slightly higher predictive value than

Table 4. Clinical Airway Predictors for Obstructive Sleep Apnoea

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^2)	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

NPV: negative predictive value; PPV: positive predictive value; ROC: receiver operating charateristics

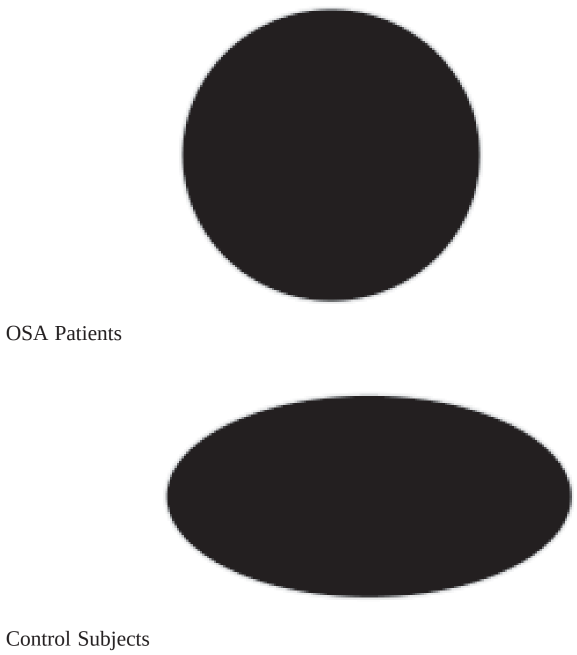


Fig. 5. Retro-palatal airway configurations in males (P <0.05). Diagrammatic representations (not in scales).

at the erect position in both resting area and Mueller's manoeuvre measurements.

In addition, a further step was taken to pursue enhanced predictability with higher precision (higher PPV and NPV values) for the retro-palatal and retro-lingual levels for both males and females by means of statistical modelling/ formulas, which were derived from logistic regression. For males, the retro-palatal predictive formula involved AS1M, LDS1M and TDS1M – the ROC obtained was 0.9457. By setting the cut-off probability at 0.6, the PPV and NPV were 94.74% and 83.33%, respectively. For females, AS1M had ROC = 1, thus no formula is required. For the retro-lingual level, the predictive formula for males involved AS2M, LDS2M and TDS2M – the ROC obtained was 0.8401. By setting the cut-off probability at 0.5, the PPV and NPV were 80.43% and 80%, respectively. No female retro-lingual formula was required as the single predictor, TDE2M, already had excellent ROC of 0.9056 and PPV of 100% and NPV of 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 retro-palatal and retro-lingual levels, during quiet respiration and Mueller's manoeuvre, 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 2). In males, it was found that the configuration of upper airway at retro-palatal 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 <0.05) (Fig. 5). At the retro-lingual level, the configurations of upper airway 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 >0.05) were similar. In females, it was found that the configuration of the upper airway at the retro-palatal 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 >0.05). At the retro-lingual level, the configurations of

Table 5. Correlations of Upper Airway Parameters with Severity of OSA

Correlations (Males)	AHI	*P*
AE1	-.190	0.161
AE1M	**-.422**	**0.001**
AE2	-.035	0.799
AE2M	-.247	0.067
AS1	-.237	0.078
AS1M	**-.639**	**<0.001**
AS2	-.148	0.275
AS2M	-.243	0.071
TDE1	**-.354**	**0.007**
TDE1M	**-.492**	**<0.001**
TDE2	-.015	0.912
TDE2M	**-.387**	**0.003**
TDS1	**-.431**	**0.001**
TDS1M	**-.540**	**<0.001**
TDS2	-.140	0.304
TDS2M	-.240	0.075
LDE1	-.025	0.852
LDE1M	**-.338**	**0.011**
LDE2	-.028	0.840
LDE2M	-.066	0.627
LDS1	-.095	0.488
LDS1M	**-.476**	**<0.001**
LDS2	-.113	0.407
LDS2M	-.056	0.682
CAE1	**.483**	**<0.001**
CAE2	**.360**	**0.004**
CAS1	**.611**	**<0.001**
CAS2	.178	0.169
CTDE1	**.475**	**<0.001**
CTDE2	**.437**	**<0.001**
CTDS1	**.453**	**<0.001**
CTDS2	.184	0.155
CLDE1	**.462**	**<0.001**
CLDE2	.028	0.832
CLDS1	**.557**	**<0.001**
CLDS2	.050	0.704
TD_LD_E1	**-.353**	**0.008**
TD_LD_E2	-.016	0.905
TD_LD_S1	**-.405**	**0.002**
TD_LD_S2	-.003	0.981

AHI: apnoea-hypopnoea index; OSA: obstructive sleep apnoea

upper airway between the normal subjects (mean TD/LD ratio was 1.0640 at E2, 1.1770 at S2) and OSA patients (mean TD/LD ratio was 1.0223 at E2, 1.1072 at S2) were similar (*P* >0.05).

In this study, we also examined correlations of various parameters of upper airway with the severity of the OSA in term of AHI index (Table 5). For males, we analysed 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

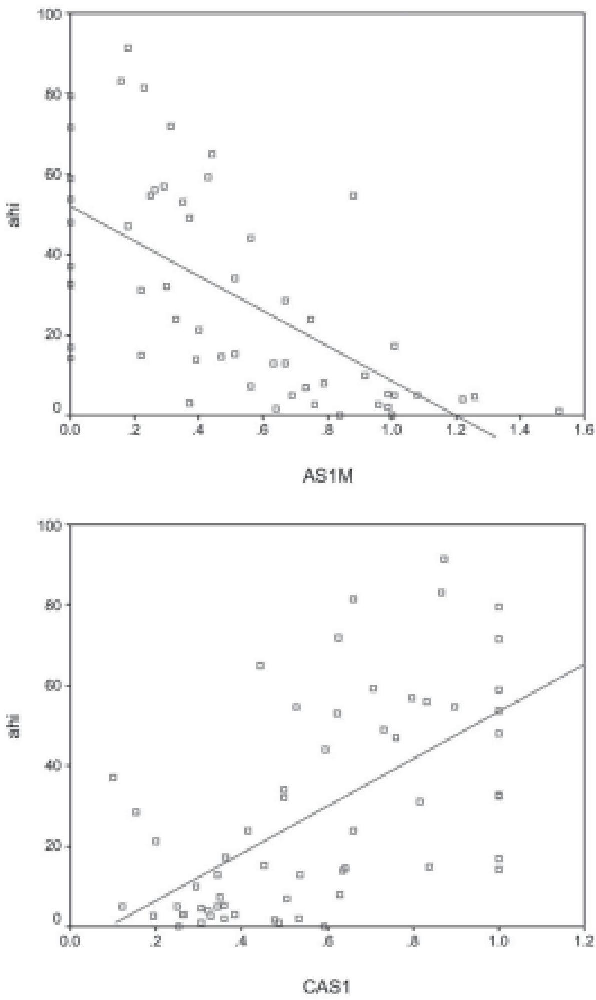


Fig. 6. Correlations between severity of OSA (AHI) and AS1M, CAS1 in OSA males.

two parameters have good correlation with the severity of OSA in term of AHI. The two parameters are AS1M and CAS1 (Fig. 6). Each of these 2 parameters has a correlation coefficient (R) value of >0.6 and a *P* value <0.05. Earlier in this study, AS1M was observed to be an excellent marker for predicting OSA at the retro-palatal level. Coupled with its good correlation with the severity of AHI, it can be concluded that AS1M is an outstanding marker for the presence and severity of OSA disease at the retro-palatal level.

In general, collapsibility parameters have positive R values, i.e., the higher the collapsibility parameter, the higher the AHI (Table 5). On the other hand, absolute dimensions have negative R values (correlations), indicating that the larger the airway dimensions, the smaller the AHI indices. It is also observed that for absolute dimensions, those done during Mueller's manoeuvre have a stronger correlation with AHI severity than those done at resting phase (quiet respiration).

We did not perform the correlation study on the female group as sample size was smaller with much less significant results.

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 radiological, e.g., cephalometric. Clinical predictors can be further sub-divided 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 inter-observer variability. The modified Mallampati 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 retro-palatal morphology.

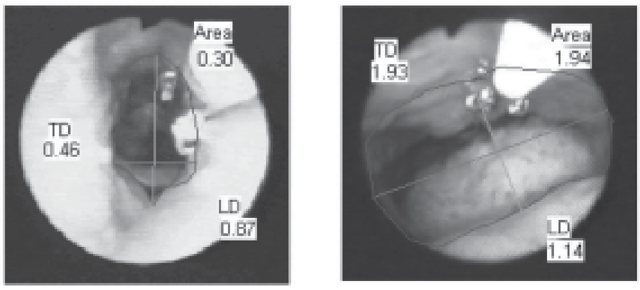


Fig. 7a. Surgical outcome assessment level 1: modified uvulopalatal advancement flap and lateral pharyngoplasty 3 months postoperatively. Note that increase in TD (320%), LD (31%), area (546%) and decrease in collapsibility and return to normal airway configuration (horizontal-oval shape in Figure 5).

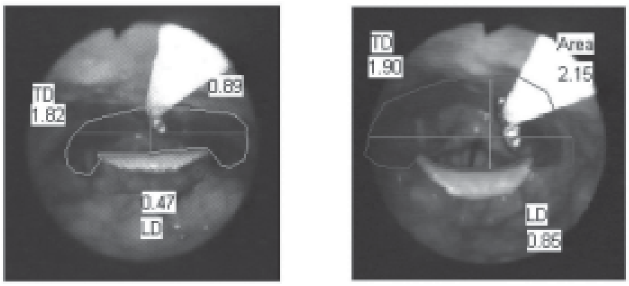


Fig. 7b. Surgical outcome assessment level 2: genioglossal advancement and radiofrequency of tongue base (somoplasty) 3 months postoperatively. Note that increase in TD (4.4%), LD (81%), area (142%) and decrease in collapsibility. Vocal cords and laryngeal inlet were not clearly visualised preoperatively and were clearly visualised postoperatively.

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. On the other hand, Mueller's studies, using dimensions obtained during Mueller's manoeuvre 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. Based on this study, it was concluded that Mueller's measurements are more useful than static ones in predicting OSA.

As an aid in upper airway assessment, the Mueller's manoeuvre 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 manoeuvre by using a five-point scale scored by different independent examiners in order to achieve an objective and reproducible upper airway assessment. They found that the severity of sleep-disordered breathing based on AHI is correlated with the Mueller's manoeuvre. Most of these investigators graded their findings based on a visual estimation of the ratio of collapsibility in terms of percentage decrease in retro-palatal diameter. These take into account only one dimension, which contributes to the retro-palatal area. It was shown in this study that the direction of collapse and the final shape of the retro-palatal 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 realised 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, 2 sets of anatomical values with excellent predictive value for both males and females were selected. For males, AS1M of <0.7981 cm^2 for the retro-palatal level and AS2M of <2.0648 cm^2 for the retro-lingual level were selected. AS1M and CAS1 were also found to have good correlations with severity of OSA. For females, AS1M of <0.522 cm^2 for the retro-palatal level and TDE2M of <1.1843 cm for the retro-lingual level were selected. Logistic regression derived formulas mentioned earlier 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 allows surgeons to plan treatment accordingly. Airway measurements with this quantitative videoendoscopy during sleep would be more physiological and realistic in nature, therefore it should be considered in our future study. Based on this study alone, there may not be sufficient information to recommend a specific surgical procedure. We can surmise that patients who meet retro-palatal criteria for OSA would benefit from palatal surgery and similarly for retro-lingual criteria. Earlier studies on 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 the upper airway morphology and dynamics to rationalise, modify and improve current surgical procedures (Fig. 7), so that we would be able to treat the obstructive sites with minimum surgery, maximum precision and effectiveness.

Conclusion

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

REFERENCES

1. Young TPM, Dempsey J, Skatrud J. The occurrence of sleep disordered breathing among middle aged adults. N Engl J Med 1993;328:1230-5.
2. Friedman M, Tanyeri H, La Rosa M. Clinical predictors of obstructive sleep apnoea. Laryngoscope 1999;109:1901-7.
3. Woodson BT, Conley SF, Dohse A, Feroah TR, Sewall SR, Fujita S. Posterior cephalometric radiographic analysis in obstructive sleep apnoea. Ann Otol Rhinol Laryngol 1997;106:310-3.
4. Yao M, Utley DS, Terris DJ. Cephalometric parameters after multilevel pharyngeal surgery for patients with obstructive sleep apnoea. Laryngoscope 1998;108:789-95.
5. Woodson BT, Wooten MR. Comparison of upper-airway evaluations during wakefulness and sleep. Laryngoscope 1994;104:821-8.
6. Hsu PP. A new method of evaluation of upper airway in patients with OSA – computer-assisted quantitative videoendoscopic analysis. Ann Acad Med Singapore 2002;31:393-8.
7. Sher AE, Thorpy MJ, Shprintzen RJ, Spielman AJ, Burack B, McGregor AP. Predictive value of Mueller manoeuvre in selection of patients for uvulopalatopharyngoplasty. Laryngoscope 1985;95:1483-7.
8. Ritter CT, Trudo FJ, Goldberg AN, Welch KC, Maislin G, Schwab RJ. Quantitative evaluation of the upper airway during nasopharyngoscopy with the Mueller's manoeuvre. Laryngoscope 1999;109:954-63.
9. Terris D, Hanasono M, Liu M. Reliability of the Mueller's manoeuvre and its association with sleep-disordered breathing. Laryngoscope 2000;110:1819-23.
10. Katsantonis GP, Maas CS, Walsh JK. The predictive efficacy of the Muller manoeuvre in uvulopalatopharyngoplasty. Laryngoscope 1989;99:677-680.
11. Petri N, Suadicani P, Wildschiodtz G, Bjorn-Jorgensen J. Predictive value of Muller manoeuvre, cephalometry and clinical features for the outcome of uvulopalatopharyngoplasty. Acta Otolaryngol 1994;114:565-71.