

## SLEEP DISORDERED BREATHING

# Craniofacial profile in Asian and white subjects with obstructive sleep apnoea

B Lam, M S M Ip, E Tench, C F Ryan

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See end of article for authors' affiliations

Correspondence to:  
Dr C F Ryan, UBC  
Respiratory Clinic,  
Vancouver General  
Hospital, 2775 Heather  
Street, Vancouver, BC,  
V5Z 3J5, Canada; fryan@  
interchange.ubc.ca

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**Background:** Clinical detection of structural narrowing of the upper airway may facilitate early recognition of obstructive sleep apnoea (OSA). To determine whether the craniofacial profile predicts the presence of OSA, the upper airway and craniofacial structure of 239 consecutive patients (164 Asian and 75 white subjects) referred to two sleep centres (Hong Kong and Vancouver) were prospectively examined for suspected sleep disordered breathing.

**Methods:** All subjects underwent a history and physical examination with measurements of anthropometric parameters and craniofacial structure including neck circumference, thyromental distance, thyromental angle, and Mallampati oropharyngeal score. OSA was defined as an apnoea-hypopnoea index (AHI) of  $\geq 5$ /hour on full overnight polysomnography.

**Results:** Discriminant function analysis indicated that the Mallampati score ( $F=0.70$ ), thyromental angle ( $F=0.60$ ), neck circumference ( $F=0.54$ ), body mass index ( $F=0.53$ ), and age ( $F=0.53$ ) were the best predictors of OSA. After controlling for ethnicity, body mass index and neck circumference, patients with OSA were older, had larger thyromental angles, and higher Mallampati scores than non-apnoeic subjects. These variables remained significantly different between OSA patients and controls across a range of cut-off values of AHI from 5 to 30/hour.

**Conclusions:** A crowded posterior oropharynx and a steep thyromental plane predict OSA across two different ethnic groups and varying degrees of obesity.

Structural narrowing of the upper airway is a major factor contributing to pharyngeal occlusion during sleep in the obstructive sleep apnoea-hypopnoea syndrome (OSAHS).<sup>1</sup> Patients with OSAHS manifest a spectrum of abnormalities of craniofacial soft tissue and skeletal anatomy that appear to act synergistically to promote upper airway obstruction during sleep.<sup>2</sup> Adiposity in the neck region and retrognathia are recognised risk factors for OSAHS.<sup>3–5</sup> Many patients with OSAHS have evidence of both neck adiposity and skeletal abnormalities.<sup>2</sup> The relative contributions of soft tissue and skeletal abnormalities vary among patients and between ethnic groups: Asians have more pronounced skeletal abnormalities and are less obese than white subjects for a given degree of severity of OSAHS.<sup>6</sup>

Epidemiological data demonstrating the relationship between OSAHS and cardiovascular morbidity highlight the potential importance of early recognition and treatment.<sup>7</sup> Yet, despite recent advances in the diagnosis and treatment of sleep disordered breathing, OSAHS remains under-recognised. This may be partly related to the limited availability of diagnostic facilities and to the non-specific nature of symptoms associated with OSAHS. Various attempts to use diagnostic algorithms based on features of the history, physical examination, and overnight oximetry to identify patients with OSAHS have met with limited success.<sup>8,9</sup> Common symptoms such as snoring and daytime hypersomnolence lack specificity for the diagnosis of OSAHS. Witnessed apnoea is an important clue but requires observation by a regular bed partner. Oximetry is widely used as a case selection tool for OSA, but its sensitivity and specificity in predicting OSA are quite variable.<sup>8</sup> Prediction models based on physical findings have used measurements that may not be easily incorporated into the routine physical examination.<sup>10</sup> Some readily detectable visual cues to the presence of OSAHS would be useful for the primary care

physician whose encounters with patients may be brief and infrequent.

In a preliminary report we observed that certain characteristics of craniofacial structure were commonplace in patients with OSAHS and could be readily identified on routine physical examination.<sup>11</sup> We therefore hypothesised that a simple clinical assessment of craniofacial profile using measurements of soft tissue and skeletal abnormalities that may contribute to upper airway narrowing would predict the presence of OSAHS. We also wished to determine whether ethnicity affected the utility of this assessment.

Some of the results of this study have been previously reported in the form of an abstract.<sup>12</sup> The study was reviewed and approved by the ethics review boards of our respective institutions.

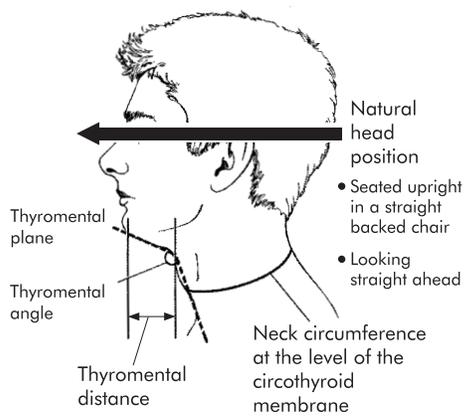
## METHODS

We studied 239 consecutive patients referred for the assessment of possible OSAHS to two university based regional sleep disorders clinics—one in Hong Kong and the other in Vancouver, British Columbia—between January and December 1999. At the time of the initial visit, having given written informed consent, each patient underwent a detailed history and physical examination including anthropometric measurements—height, weight, and calculation of body mass index (BMI).

## Craniofacial measurements

Craniofacial measurements were made with the patient seated upright in a straight backed chair in the natural head position looking straight ahead (fig 1). Natural head position

**Abbreviations:** AHI, apnoea-hypopnoea index; BMI, body mass index; MS, Mallampati score; NC, neck circumference; OSA, obstructive sleep apnoea; OSAHS, obstructive sleep apnoea-hypopnoea syndrome; TMA, thyromental angle; TMD, thyromental distance



**Figure 1** Profile of the head and neck region illustrating the following features: thyromental plane: running through the soft tissue mentum and the thyroid prominence; thyromental angle (TMA): between the thyromental plane and the soft tissue plane of the anterior neck; thyromental distance (TMD): the horizontal distance between the thyroid prominence and a perpendicular dropped from the soft tissue mentum; neck circumference (NC): at the level of the cricothyroid membrane.

is used increasingly as a logical reference for the evaluation of craniofacial morphology and has been shown to be stable and reproducible in the short term to within 2°. The following measurements were made:

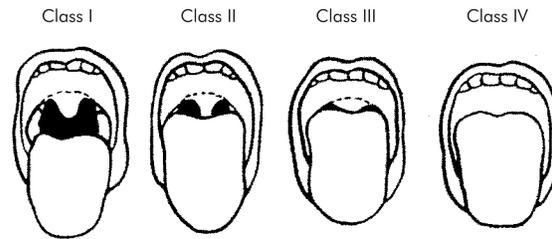
- Neck circumference (NC): at the level of the cricothyroid membrane, measured with a tape measure.
- Thyromental distance (TMD): the horizontal distance from the thyroid prominence to a perpendicular dropped from the soft tissue mentum, measured with a modified tape measure with a vertical attachment.
- Thyromental angle (TMA): the angle between the soft tissue plane of the anterior neck and a plane running through the soft tissue mentum and the thyroid prominence, measured from a lateral photograph of the head and neck taken in the natural head position with the patient looking straight ahead. The camera was mounted on a tripod with the front of the lens oriented vertically, at a constant distance of 6 feet from the patients' left ear and with the height adjusted to maintain the body of the lens horizontal, centred on the tragus of the left ear.
- Mallampati oropharyngeal score (MS):<sup>14</sup> measured during a breath hold at end-tidal inspiration with the mouth wide open, tongue maximally protruded, but without phonation or attempted elevation of the soft palate (fig 2).

### Reliability of measurements

A training session was held at one centre before study commencement during which the measurement techniques for all variables were standardised. Measurements were performed by a single investigator at each centre (CFR and BL). Intra-observer agreement was assessed for MS, NC, and TMD in a sample of 20 patients. On a sample of 50 randomly selected patients, tests of intra- and inter-observer agreement were performed for the measurement of TMA. For intra-observer reliability, measurements were made in random order on two occasions separated by several days. For inter-observer reliability, measurements were made at one centre and repeated in random order on duplicate images at the other centre in a blinded fashion.

### Polysomnography

Each patient had full overnight polysomnography within 12 weeks of the initial assessment, reflecting the waiting



**Figure 2** Mallampati oropharyngeal score (MS) measured during a breath hold at end-tidal inspiration with the mouth wide open, tongue maximally protruded, but without phonation or attempted elevation of the soft palate.

times in our facilities at the time of the study. Polysomnography was performed using methodology, instrumentation, and analysis standardised between both sleep centres according to the recommendations on syndrome definition and measurement techniques published by the American Academy of Sleep Medicine.<sup>15</sup> Polysomnograms were scored by technicians at the respective sites according to usual clinical practice. OSA was defined as an apnoea-hypopnoea index (AHI) of  $\geq 5$ /hour of total sleep time.

### Statistical analysis

The rationale and methodology for the statistical analysis are outlined in detail in the supplement available online at the *Thorax* website (<http://www.thoraxjnl.com/supplemental>). A summary of the analysis is given here. Spearman rank correlation, to account for outlying measurements, was used to assess intra- and inter-observer reliability in the craniofacial measurements. SPSS Version 10.0.7 was used for all other analyses. The statistical strategy in this study was to determine which clinical, anthropometric, and craniofacial variables could be broadly applied to predict which patients were more likely to have OSA. The clinical variables of interest were age, BMI, NC, MS, TMA, TMD, and Epworth Sleepiness Scale. First, three Hotelling's  $T^2$  analyses examined the relationship between (1) sex, (2) ethnic group, and (3) OSA and the clinical variables. The sample of patients was then randomly divided into two groups of 120 and 119 patients balanced with respect to sex, ethnicity, and OSA status. Discriminant function analysis was applied to the initial group of 120 patients to generate an equation using the clinical variables to predict whether a patient was more likely to have OSA or to be normal. A receiver operator characteristic curve (ROC) was also plotted to assess the equation in terms of sensitivity and specificity and for comparison with other previously published prediction equations. The second group of 119 patients was used to perform a prospective data analysis (cross validation) to assess the performance of the equation in a different but comparable group from the one in which it was originally developed. Finally, an analysis of covariance (ANCOVA) was performed to effectively make all patients equivalent for BMI, NC, and ethnic group in order to determine whether the relationship between selected clinical variables from the discriminant analysis was still significant when the group of patients was statistically rendered equivalent on these three variables. Additionally, several different cut-offs for the definition of OSA (AHI  $\geq 5$ ,  $\geq 10$ ,  $\geq 15$ ,  $\geq 30$ ) were tested to determine whether the same variables were significant for more rigorous definitions of OSA. Summary data are presented as mean (SD).

### RESULTS

Demographic data summarised by group differences in disease category, ethnic group, and sex are shown in table 1. Of the 239 patients, 201 had OSA (AHI  $\geq 5$ ). As a group, these

**Table 1** Group differences by disease category, ethnicity and sex†

Variable	Disease category		Ethnicity		Sex	
	OSA (n = 201)	Normal (n = 38)	Asian (n = 164)	White (n = 75)	Male (n = 199)	Female (n = 40)
Age (years)	49 (12)	44 (13)	49 (11)	47 (14)	49 (12)	48 (12)
M/F	169/32	30/8	140/24	59/16	—	—
BMI (kg/m <sup>2</sup> )	29 (5)	27 (5)	29 (4)	30 (7)	29 (5)	30 (7)
Neck (cm)	40 (4)	39 (4)	40 (3)	41 (4)	41 (3)	36 (4)*
MS (1–4)	3.7 (0.5)	3.4 (0.8)*	3.9 (0.4)	3.2 (0.8)*	3.7 (0.6)	3.5 (0.6)
TMA (degrees)	161 (18)	149 (19)*	161 (18)	156 (19)	160 (18)	155 (22)
TMD (cm)	5 (1)	5 (1)	5 (1)	6 (1)*	5 (1)	5 (1)
ESS	11 (5)	11 (5)	11 (5)	11 (5)	11 (5)	11 (6)
AHI (/h)	32 (22)	3 (2)*	30 (24)	22 (19)	30 (23)	14 (13)*

OSA, obstructive sleep apnoea; BMI, body mass index; MS, Mallampati oropharyngeal score; TMA, thyromental angle; TMD, thyromental distance; ESS, Epworth Sleepiness Scale; AHI, apnoea-hypopnoea index.

Values are mean (SD).

\*p value <0.001.

†Following Bonferroni corrections for multiple comparisons, p values ≤0.006 were considered significant.

patients were middle aged (49 (12) years), moderately obese (BMI 29.5 (6.3) kg/m<sup>2</sup>), and had moderate to severe OSA (AHI 31.9 (22.2)/h). All of the Hong Kong subjects (n = 154) and 10 of the Vancouver subjects were Asian; the remaining 75 Vancouver subjects were white. The majority (83%) were male. There was no change in body weight between the performance of the anthropometric measurements and the polysomnogram.

Spearman rank correlation indicated intra-observer agreement (confidence intervals) of 0.81 (0.56 to 0.92) for MS; 0.97 (0.93 to 0.99) for NC; and 0.85 (0.71 to 0.90) for TMD. For TMA, intra-observer agreement was 0.91 (0.87 to 0.94) and inter-observer agreement was 0.83 (0.71 to 0.90). Values greater than 0.80 indicate acceptable reliability.

**Hotelling’s T<sup>2</sup> analyses of OSA and clinical variables**

The results of the initial T<sup>2</sup> analyses (OSA defined as AHI ≥5) of the full demographic data set are provided in table 1. Patients with OSA had higher MS, larger TMA, and higher AHI than subjects without OSA. Asians had higher MS and shorter TMD than whites. Men had larger NC and higher AHI than women. Although the proportion of women was somewhat greater among whites, this was not significant. Because of their small numbers, it was not possible to repeat the same analyses on the women as a subgroup. When women were excluded from the analysis, there were no differences in the overall results when comparing groups by disease category or ethnicity, or in the multivariate analyses.

**Discriminant analysis**

From the preceding analyses a subset of potentially useful predictor variables including TMA, MS, age, BMI, NC and TMD was selected for a discriminant analysis. This analysis confirmed that these variables could be used to discriminate

**Table 2** Discriminant function analysis for the prediction of OSA (AHI ≥5)†

Variable	Function
Mallampati score	0.70*
Thyromental angle	0.60*
Neck circumference	0.54*
Body mass index	0.53*
Age	0.53*
Thyromental distance	−0.13

\*Significant correlation.

†Correlation between clinical variables and discriminant function for the initial sample of 120 patients split by OSA.

**Table 3** Prediction equations for the presence or absence of OSA (AHI ≥5)\*

Variable		OSA	Normal
Mallampati score	×	(7.135)	(6.227)
+			
Thyromental angle	×	(0.171)	(0.163)
+			
Neck circumference	×	(2.883)	(2.758)
−			
Body mass index	×	(0.075)	(0.163)
+			
Age	×	(0.166)	(0.131)
+			
Thyromental distance	×	(102.571)	(92.088)
=		OSA score	Normal score

\*A patient’s score is calculated for both equations by multiplying the raw score for each coefficient and summing these products. The larger score indicates the group to which the patient more likely belongs.

between patients with OSA and normal subjects. The size of each correlation (function) described in table 2 reveals the strength of the relationship between that predictor and OSA. Patients with OSA had, in order of importance, significantly higher MS, larger TMA, larger NC, higher BMI, and were older than normal subjects. An equation was derived from this analysis to categorise patients as either OSA or normal (table 3). When this equation was applied to the initial set of 120 patients from which it was derived, it correctly classified 86% of the patients. When applied prospectively to the second set of 119 patients its performance was comparable, correctly classifying 82% of patients as either OSA or normal.

**Analysis of covariance (ANCOVA)**

Following the positive results of the discriminant analysis, the data from the 120 and 119 patients were again pooled for the ANCOVA. The purpose of the ANCOVA was to examine the relationship between OSA and MS, TMA, TMD, and age after statistically removing prior differences in three potentially important confounding variables—BMI, NC, and ethnic group. By treating ethnic group as an independent variable rather than a covariate, differences between ethnic groups could also be examined separately after removing prior differences in BMI and NC. BMI was significantly related to the set of dependent variables, as was NC and ethnic group (p<0.05). Thus, these three variables could be used to statistically render patients as if they had all scored equally on these variables. It is notable that there was no interaction between OSA and ethnic group. The relationship between

**Table 4** Comparisons between subjects with OSA and normal subjects for different cut off values for apnoea-hypopnoea index after adjustment for BMI, neck circumference, and ethnicity†

AHI(/h)	Age (years)			Mallampati score (1–4)			Thyromental angle (degrees)		
	OSA	Normal	p value	OSA	Normal	p value	OSA	Normal	p value
≥5	49	44	*	3.7	3.4	*	161	151	*
n	(201)	(38)							
≥10	50	46	*	3.7	3.5	*	161	154	*
n	(168)	(71)							
≥15	50	46	*	3.8	3.5	*	161	156	*
n	(143)	(96)							
≥30	51	47	*	3.8	3.6	*	164	157	*
n	(88)	(151)							

Values are means.

\* $p < 0.05$ .

†ANCOVA with adjustment for BMI, neck circumference and ethnicity; Bonferroni corrections for multiple comparisons; and follow-up univariate analyses.

OSA and age, MS, TMA and TMD could therefore be examined without regard to ethnic group; also investigation of ethnic group could proceed independently of OSA status. In addition, we were interested in determining whether the relationship remained stable using varying cut off levels of AHI to define OSA ( $\geq 5$ ,  $\geq 10$ ,  $\geq 15$ , and  $\geq 30$ ).

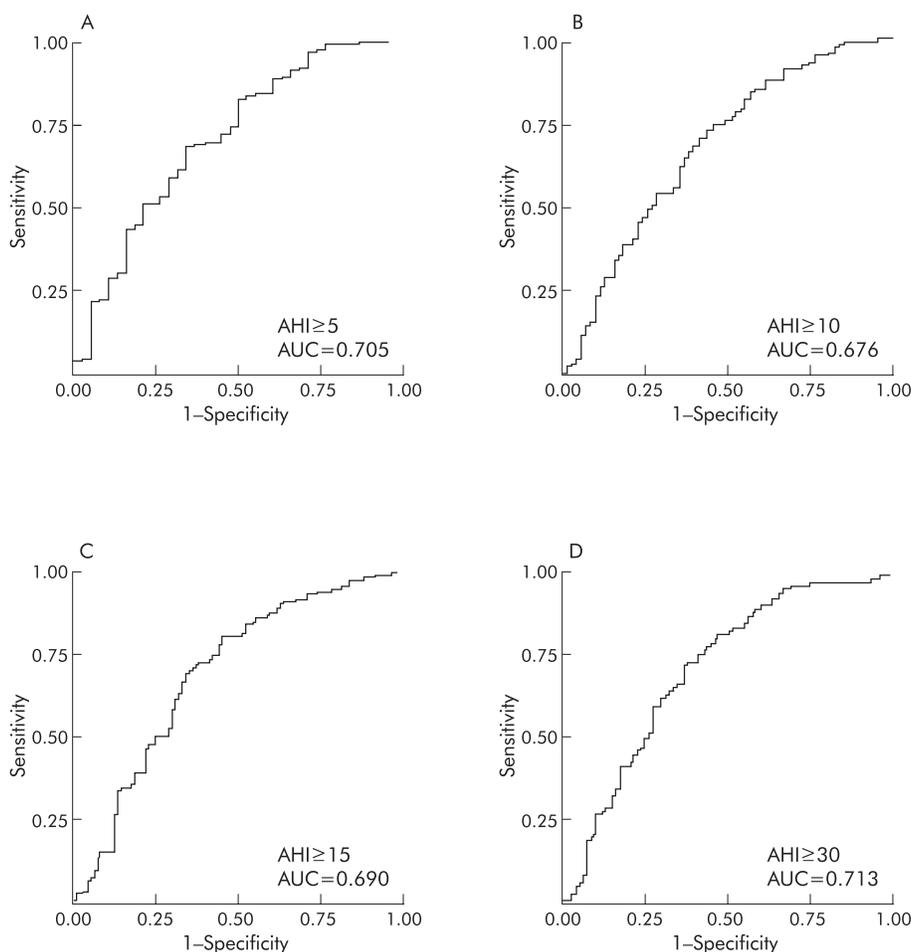
### OSA

The set of dependent variables was related significantly to OSA ( $p < 0.05$ ). Follow up ANOVAs, with Bonferroni corrections to control the error rate, showed that age, MS, and TMA

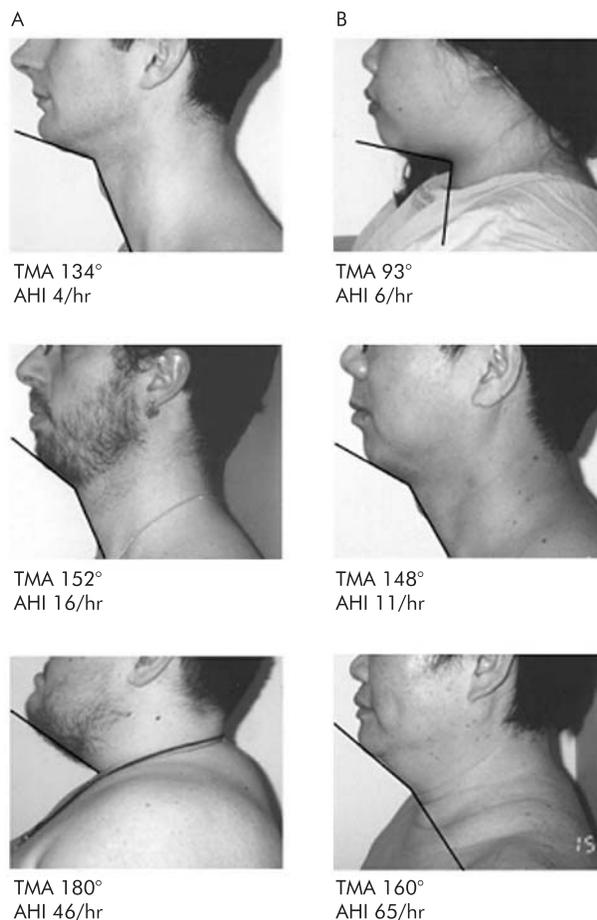
distinguished patients with OSA from normal subjects ( $p < 0.05$ ). In order of importance, these comparisons revealed that OSA patients were older than normal subjects ( $M = 49.27$  v  $44.08$ ), had larger TMA ( $M = 161.17$  v  $148.92$ ) and had higher MS ( $M = 3.71$  v  $3.37$ ).

### Ethnic group

After removal of prior differences in BMI and NC, Asians differed from whites in MS, TMD and TMA. In order of importance, Asians had higher MS, smaller TMD, and larger TMA than white subjects ( $p < 0.05$ ).



**Figure 3** Receiver operator characteristic curves for the predictive equations using different cut off values of apnoea-hypopnoea index (AHI) for the definition of obstructive sleep apnoea: (A)  $AHI \geq 5$ , (B)  $AHI \geq 10$ , (C)  $AHI \geq 15$ , (D)  $AHI \geq 30$ . AUC = area under the curve.



**Figure 4** Lateral photographs of the head and neck region showing examples of the thyromental angle in (A) white and (B) Asian patients with varying degrees of severity of obstructive sleep apnoea. TMA = thyromental angle (degrees); AHI = apnoea-hypopnoea index (/hour).

### Varying definitions of OSA

For each definition of OSA (AHI  $\geq 5$ ,  $\geq 10$ ,  $\geq 15$ , and  $\geq 30$ ), increasing age, MS, and TMA were significantly associated with the presence of OSA (table 4). ROC curves of the predictive equations for different degrees of OSA severity are shown in fig 3. The area under the curve (AUC) was similar for each cut off (0.705 for AHI  $\geq 5$ ; 0.676 for AHI  $\geq 10$ ; 0.696 for AHI  $\geq 15$ ; and 0.713 for AHI  $\geq 30$ ). Figure 4 shows examples of the TMA measurement in white and Asian patients with different degrees of severity of OSA.

### DISCUSSION

Our results indicate that patients with OSA of differing ethnicity and varying degrees of obesity have a crowded posterior oropharynx and a steep thyromental plane compared with non-apnoeic controls. After accounting for ethnic group, BMI and NC, patients with OSA are older and have larger MS and TMA. These craniofacial features probably reflect structural narrowing of the upper airway that contributes directly to the pathogenesis of upper airway obstruction in OSA. A crowded posterior oropharynx and a steep thyromental plane appear to be particularly useful clinical markers of OSA since they remain strong predictors even after correction for two important confounding variables—ethnicity and obesity—and over a wide range of cut-off values for the definition of OSA.

Whether clinical features can be reliably used to predict OSA among suspected individuals is still controversial.<sup>16–18</sup>

Ross and co-workers<sup>8</sup> conducted a systematic review and meta-analysis of the literature regarding the diagnosis of OSA. Among the articles reviewed were eight studies reporting prediction equations. The pooled estimates of these models were 66.5 (14)% for sensitivity and 88.7 (4.9)% for specificity. Rowley and colleagues prospectively evaluated four clinical prediction equations for the diagnosis of OSA and the prioritisation of patients for polysomnography.<sup>9</sup> The performance characteristics of these equations were similar with AUCs ranging from 0.669 to 0.736, comparable to those of the ROC curves for the prediction equation in our study. The authors concluded that these models could be used as part of a clinical pathway to prioritise patients for polysomnography.

Several craniofacial characteristics have been shown to be associated with the development and severity of sleep disordered breathing. The most commonly reported abnormalities include an inferiorly positioned hyoid bone, a posteriorly placed maxilla and mandible, an enlarged tongue and soft palate, and a smaller velopharyngeal cross sectional area.<sup>19–23</sup> These craniofacial abnormalities have been reported in both white and Asian patients with OSAHS.<sup>24–25</sup> Their measurement, however, requires the use of imaging modalities such as cephalometry and computed tomography, thus limiting their clinical utility. Most previous prediction models based on clinical variables have failed to include craniofacial measurements.

Few studies have reported the use of clinically derived craniofacial measurements in the prediction of OSA. Kushida and colleagues reported the development of a model based on BMI, NC, and oral cavity measurements.<sup>10</sup> This model had a sensitivity of 97.6% and a specificity of 100% for the detection of OSA based on an AHI of  $\geq 5$ . The prevalence of OSA in the study by Kushida *et al* was 85% and analyses for different cut-off values for AHI were not performed. The results were strongly influenced by the large difference in BMI between patients with OSA and controls. This model required the performance of several complicated intraoral measurements using calipers, and it is questionable whether it would be suitable for routine clinical use. Friedman and colleagues examined the utility of various clinical features including upper airway measurements that predict a difficult endotracheal intubation.<sup>26</sup> In a study of 172 patients they found that a modified MS, tonsil size and BMI (but not TMD) were predictive of OSA. In combination, these measurements accounted for 20% of the variance in respiratory disturbance index (RDI). Their analysis did not account for the potential interaction between BMI and the upper airway variables. Schellenberg and associates<sup>27</sup> investigated several upper airway bony and soft tissue structural abnormalities for their ability to predict OSA after adjustment for important confounding factors. In a cohort of 420 subjects they measured the presence or absence of enlargement of the tonsils, uvula and tongue, low lying soft palate, retrognathia, overjet, and lateral pharyngeal narrowing. After adjusting for BMI and NC, only lateral pharyngeal narrowing and tonsillar enlargement were associated with OSA. Skeletal features such as overjet and retrognathia were not significant predictors. A subgroup analysis of women yielded no significant associations, probably as a consequence of the small sample size. In that study one investigator performed all the morphometric measurements and intra and inter-observer agreement were not assessed.

We chose simple clinical measurements of upper airway morphology such as the MS, TMD, and TMA because they are easy to perform. The MS has been used by anaesthetists for many years to help predict the degree of difficulty of endotracheal intubation.<sup>14</sup> It reflects the amount of soft tissue in the posterior oropharynx relative to its skeletal

constraints. The TMD represents the position of the chin relative to the thyroid cartilage and may be related to the length of the anterior cranial base. The MS and TMD have been shown to correlate with both difficult endotracheal intubation and OSA.<sup>26–28</sup> The TMA has not been reported previously. To obtain an objective measurement of this feature of the craniofacial profile for the purpose of this study, we chose to determine the TMA from a lateral photograph of the head and neck obtained in a standardised fashion. We believe this angle reflects features of both obesity and abnormal craniofacial skeletal structure. Central obesity with accumulation of adipose tissue in the submental region will result in a large TMA. A short TMD or anterior cranial base will also result in a large TMA. Since the majority of patients with OSA have evidence of both obesity and craniofacial abnormalities,<sup>2</sup> it is not surprising that TMA emerged as a significant predictor of OSA in our study. A high MS indicates a crowded posterior oropharynx which can be caused by obesity or craniofacial abnormality, or a combination of both. The predictive value of a large TMA and a high MS—after adjusting for ethnicity, BMI and NC, and for different AHI cut-off values for the definition OSA—indicates a strong relationship between these two measurements and OSA. Both BMI and NC have previously been shown to correlate well with OSA, and both emerged as significant variables in our predictive equation, although less so than MS and TMA. Symptoms were not included in our predictive equation; a previous study found that they do not differentiate reliably between patients with and without OSA.<sup>29</sup> Our results show that a simple clinical assessment of anthropometric features and craniofacial structure can help predict the presence of OSA.

Tsai and associates recently developed a decision rule for the diagnosis of OSA based on similar features of upper airway morphology including cricomental space (the perpendicular distance to the skin of the neck from the midpoint of a line joining the cricoid to the mentum); pharyngeal grade (similar to the MS); and overbite.<sup>30</sup> Use of the decision rule allowed these investigators to confidently confirm or exclude OSA in 44% of patients. These results, together with our data, strongly suggest that clinical measurements from the craniofacial profile are good candidates for inclusion in the development of clinical prediction algorithms for the diagnosis of OSA and the prioritisation of patients for polysomnography. Our results extend the potential utility of these simple clinical measurements by demonstrating their applicability to patients of differing ethnicity and degrees of obesity.

We found that Asians had higher MS, shorter TMD and larger TMA, and tended to have more severe OSA than white subjects. Although the shorter TMD might suggest retrognathia, previous studies have shown that Asians have a more protruded maxilla and mandible.<sup>31</sup> We suspect that the shorter TMD in Asians may be explained by a shorter anterior cranial base reflecting their smaller anteroposterior facial dimensions.<sup>32</sup> Li and associates compared two consecutive series of 50 Asian and 50 white men with OSA.<sup>6</sup> When matched for obesity, Asians had more severe OSA than whites. After controlling for the severity of OSA, Asians were less obese than whites and had a more anteriorly positioned maxilla and mandible but a shorter anterior cranial base dimension ( $p < 0.0001$ ). Although the TMD did not differ between patients with OSA and normal controls in our study, the shorter TMD in Asians could contribute to a larger TMA and steeper thyromental plane in patients with OSA in this ethnic group. The higher MS and shorter TMD in Asians may reflect abnormalities of craniofacial anatomy that contribute to structural narrowing of the upper airway independent of obesity. The higher MS in Asians, reflecting more severe

posterior oropharyngeal narrowing, might also explain why Asian men have more severe OSA than white men when matched for age and BMI.<sup>6</sup> A few of our subjects (17%) were women and, as shown in previous studies, they had smaller neck circumferences and less severe OSA than the men. The TMA and MS did not differ significantly between men and women.

Our study has certain limitations that may have an impact on the generalisability of our findings. There was a high prevalence of OSA in our sample, as defined by our a priori definition of  $AHI \geq 5$ . We chose this definition to correspond with the generally accepted criteria proposed by the American Academy of Sleep Medicine.<sup>15</sup> We performed post hoc analyses using different definitions for OSA which indicated that the predictive variables retained their utility over a wide range of cut-off values for AHI. Furthermore, discriminant analysis allows one to specify that prior probabilities are based on actual rather than equal group sizes, thus avoiding the problem of spuriously increased specificity. We studied only Asians and whites, so our results may not be applicable to other ethnic groups. There is a clear need for more data on the manifestations of sleep disordered breathing in different ethnic groups.

In conclusion, we have shown that risk factors for OSA such as obesity and craniofacial features that reflect structural narrowing of the upper airway are readily identified and can easily be incorporated into the routine physical examination. Patients with OSA of differing ethnicity and varying degrees of obesity have a crowded posterior oropharynx and a steep thyromental plane. Recognition of these abnormalities in the craniofacial profile should alert the physician to the possibility of OSA.



Details of the rationale and methodology for the statistical analysis are shown in the supplement available online at the *Thorax* website (<http://www.thoraxjnl.com/supplemental>).

#### Authors' affiliations

**B Lam, M S M Ip**, University of Hong Kong, Hong Kong SAR, China  
**E Trench, C F Ryan**, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

Supported by British Columbia Lung Association

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## **Online Supplement**

### **Craniofacial Profile in Asians and Caucasians with Obstructive Sleep Apnea**

**Bing Lam, Mary S.M. Ip, Elizabeth Tench, C. Frank Ryan**

#### **Statistical analysis**

##### **Framework for Statistical Analysis**

Thorough preliminary data checks determined that the dataset of 239 patients was suitable for multivariate analyses (Tabachnick & Fidell, 2000). Spearman Rank Correlation was used to assess intra- and inter-observer reliability in the craniofacial measurements. SPSS Version 10.0.7 was used for all other analyses. Conservative significance levels were selected in all analyses to reduce error. The statistical strategy was to determine which dependent clinical and upper airway anthropometric variables could be broadly applied to predict which patients were likely to have obstructive sleep apnea (OSA). The dependent variables were age, body mass index (BMI), neck circumference (NC), Mallampati Score (MS), thyro-mental angle (TMA), thyro-mental distance (TD), Epworth Sleepiness Scale (ESS), and apnea-hypopnea index (AHI). Three sets of analyses were performed.

First we performed Hotelling's  $T^2$  tests on three independent variables measuring subgroups of special interest – (i) OSA; (ii) gender; and (iii) ethnic group. The purpose of the Hotellings  $T^2$  analyses was to examine the relationship between these three

independent variables and the clinical dependent variables as a set without inflating error by the use of multiple t-tests.

Next, the sample of patients was divided into two groups of 120 and 119 patients, randomly selected from within groups of gender, ethnic status and OSA status to make two proportional groups. A discriminant function analysis was then applied to the first group of 120 patients to use the dependent set of variables as predictors of OSA and to thereby generate an equation for the prediction of OSA. Prior probabilities were based on actual group sizes to avoid spuriously increased specificity. A receiver operator characteristic curve (ROC) was also plotted to assess the utility of this prediction equation in terms of sensitivity and specificity and for comparison with other published prediction equations. The equation was then tested prospectively (cross-validation) in the other randomly selecting set of 119 patients to see how well the equation performed in a population other than that from which it was originally formulated.

Finally, an Analysis of Covariance (ANCOVA) was performed to effectively make all patients equivalent for BMI, NC and ethnic group, in order to determine whether the relationship between selected variables from the discriminant analysis was still significant when the patients were made equivalent on these three variables. In addition, several different cut-offs were used for the definition of OSA (AHI > 5, >10, >15, >30). Receiver operator characteristic curves were plotted to compare the accuracy of the predictive equations for the different cut-offs of OSA severity.

### **Hotelling's T<sup>2</sup> Analysis**

Three T<sup>2</sup> analyses were conducted to determine the relationship between three independent variables, (i) OSA, (ii) ethnic group and (iii) gender, and the set of dependent clinical variables including age, weight, BMI, neck circumference, Mallampati score, thyro-mental angle, thyro-mental distance, ESS (Epworth Sleepiness Scale) and AHI (Table 1. in the manuscript). In the first analysis, OSA was found to be related significantly to the set of dependent variables,  $T^2(9, 229) = 9.03$ ,  $p < 0.001$ . Patients with OSA compared with Normals had larger Mallampati scores (mean=3.71 vs 3.37); greater thyro-mental angles (mean=161.12 vs 148.92°); and higher AHI (mean=31.68 vs 2.61/h). Caucasians and Asians differed significantly on the set of dependent variables,  $T^2(9, 229)=20.67$ ,  $p < 0.001$ . Asians were lighter (mean=78.08 vs 92.18 kg) (data not included in the Table); had higher Mallampati scores (mean=3.85 vs 3.23); and shorter thyro-mental distances (mean=5.07 vs 5.62 cm) compared with Asians. In the analysis using gender as an independent variable, there was a significant relationship between gender and the set of dependent variables,  $T^2(9, 229)= 26.59$ ,  $p < 0.001$ . Males had larger neck circumferences (mean=40.68 vs 36.27 cm) and higher AHI (mean=29.78 vs 13.56/h) compared with females.

### **Discriminant Function Analysis**

The purpose of the discriminant analysis was (i) to see whether selected predictors from the Hotelling's T<sup>2</sup> analyses: age, BMI, NC, MP, TMA, and TMD, could be used to

distinguish OSA patients from Normals; and (ii) to develop an equation whereby weights could be assigned to the predictor variables in order to be of use in predicting the presence of OSA in new patients. Discriminant analysis was selected in favor of logistic analysis because in conditions where the underlying variables such as age and BMI are normally distributed, discriminant analysis can be more powerful in detecting group differences; i.e. in this study, in predicting whether patients had OSA or not (Tabachnick & Fidell, 2000). The sample of 239 patients was divided into two groups of 120 and 119 patients based on random assignment to one group or the other in roughly equal proportions of OSA and Normals, males and females, Caucasians and Asians. Tests to ensure power was adequate to predict group membership with these group sizes were satisfactory (0.80). Variance-covariance matrices were examined prior to the analyses since, if they are not approximately even for each of the OSA and Normal groups, classification problems can occur where patients would be over-classified into the group with the biggest spread in variance. In this case, the variance-covariance matrices were proportional. Expected probabilities, also known as prior probabilities, were selected for the analysis to account for the difference between the Normal and OSA group sizes. With these important preliminary analyses and specifications accounted for, the main discriminant analysis was then performed. The main purpose in splitting the sample was to use the initial sample of 120 patients to see whether the selected predictors could be used to significantly distinguish OSA patients from Normals. The second reason was to see whether the prediction equation could be applied to the predictor variable set of the 119 patients and still retain the ability to distinguish between the OSA and Normal patients. OSA was defined as  $AHI \geq 5$ . The results of the discriminant analysis indicated

that the set of clinical predictors was able to discriminate well between Normal participants and those with OSA,  $\chi^2(6) = 27.82$ ,  $p < .05$ ; and 85.8% of patients were correctly classified. In order of importance (correlations with the discriminant function appear in brackets after each variable), the best predictors of OSA were MS(0.70), TMA (0.60), NC (0.54), BMI (0.53), age (0.53), and TMD (-0.13) (Table 2. in the manuscript). TMD was below the suggested cut-off of .30 (Tabachnick & Fidell, 2000) for inclusion as a significant predictor. Examination of the means for these variables demonstrated that (means for the group with OSA appear first in brackets after each variable and the means for the group without OSA appear after the colon) participants with OSA had a higher MS ( $\underline{M}=3.71$ ;  $\underline{M}=3.37$ ), a greater TMA ( $\underline{M}=161.12$ ;  $\underline{M}=148.92$ ), a larger NC ( $\underline{M}=40.16$ ;  $\underline{M}=38.78$ ), a higher BMI ( $\underline{M}=29.42$ ;  $\underline{M}=27.29$ ), and were of greater age ( $\underline{M}=49.27$ ;  $\underline{M}=44.08$ ) than Normals. When the equation derived from the initial sample of 120 patients (Table 3 in the manuscript) was applied to the predictor variable set from the sample of 119 patients, 82.4% of patients were correctly classified. In view of the positive results of the discriminant analysis, the data from 120 and 119 patients were again pooled for the final analysis of covariance (ANCOVA).

### **Analysis of Covariance (ANCOVA)**

#### **(i) Dependent Variables Grouped by Disease Classification and Ethnic Group with Effects of BMI and Neck Circumference Removed**

An analysis of covariance (ANCOVA) of the 239 patients was conducted using age, MS, TMA and TMD as dependent variables, OSA and ethnic group as independent variables,

and BMI and NC as covariates. The purpose of the ANCOVA was to examine the relationship between OSA and the four dependent variables while statistically removing prior differences in ethnic group, BMI and NC. The intent of removing the effects of BMI, NC and ethnic group was to increase the relationship between the four dependent variables and OSA by treating all scores for the sample of 239 patients as if they had the same ethnicity, BMI and NC. This procedure removes error from the ANCOVA due to the effects of ethnic group, BMI and NC so that one is left with a clearer picture of how well age, MS, TMA and TMD are related to OSA status. Additionally, by treating ethnic group as another independent variable rather than a covariate, this approach allows differences between ethnic groups to be examined separately after removal of the effects of prior differences in BMI and NC.

BMI was significantly related to the set of dependent variables,  $F(4,230)=6.26$ ,  $p < 0.05$ , as was NC,  $F(4,230)=4.58$ ,  $p < 0.05$ , and ethnic group,  $F(4,230)=15.46$ ,  $p < 0.05$ . These findings indicated that these three variables could be used to perform the desired function of rendering patients as if they had all scored equally on these variables. It is notable that there was no interaction between OSA and ethnic group. This indicated that the relationship between OSA and age, MP, TMA and TMD could be examined without regard to ethnic group; also investigation of ethnic group could proceed independently of OSA status.

### **OSA**

The set of dependent variables was related significantly to OSA,  $F(4, 230)=4.08$ ,  $p < 0.05$ . Follow-up ANOVAs, with Bonferroni corrections to control the error rate, demonstrated that age,  $F(1,233)=9.12$ ,  $p < 0.05$ , MS,  $F(1,233)=7.59$ ,  $p < 0.05$ , and TMA,

$F(1,233)=6.11$ ,  $p<0.05$ , distinguished OSA patients from normals. These comparisons revealed that OSA patients compared with normals were older ( $M=49.27$  vs  $44.08$ ), had larger TMA ( $M=161.17$  vs  $148.92$ ), and had higher MS ( $M=3.71$  vs  $3.37$ ).

### **Ethnic group**

The significant relationship between ethnic group and the set of dependent variables was analysed to determine which of the dependent variables was related to ethnic group after adjustment for the effects of BMI and NC. ANOVAs, with Bonferroni corrections for the number of ANOVAs conducted, demonstrated that TMD,  $F(1,233)=10.07$ ,  $p<0.05$ , MS,  $F(1,233)=57.05$ ,  $p<0.05$ , and TMA,  $F(1,233)=4.01$ ,  $p<0.05$ , distinguished Caucasian and Asian groups. Ordering significant dependent variables by the magnitude of the F values indicates that the most important dependent variables separating ethnic groups were MS, TMD and TMA. These comparisons revealed that Asians compared with Caucasians had a higher MS ( $M=3.85$  vs  $3.23$ ); larger TMA ( $M=160.51$  vs  $156.40$ ); smaller TMD ( $M=5.07$  vs  $5.66$ ).

### **(ii) Analysis of Age, Mallampati Score, Thyromental Angle, and Thyromental Distance for Different Cutoff Values of AHI.**

Three ANCOVAs using different cutoffs of AHI to define OSA versus Normal were conducted to determine if there were similar effects of the dependent variables of age, MS, TMA and TMD (Table 4. in the manuscript).

**AHI  $\geq$  10**

In this ANCOVA, 168 had OSA patients while 71 were Normal. The set of dependent variables was related significantly to OSA,  $F(4,232)=3.96$ ,  $p < 0.05$ . Follow-up ANOVAs demonstrated that age,  $F(1,236)=5.52$ ,  $p < 0.05$ , MS,  $F(1,236)=7.97$ ,  $p < 0.05$  and TMA,  $F(1,236)=9.52$ ,  $p < 0.05$ , distinguished between OSA patients and Normals. The post hoc comparisons revealed that OSA patients compared with Normals were older ( $M=49.63$  vs  $45.64$ ); had higher MS ( $M=3.73$  vs  $3.49$ ); and larger TMA ( $M=161.45$  vs  $53.94$ ).

**AHI  $\geq$  15**

In this ANCOVA, 143 patients had OSA and 96 were Normal. The set of dependent variables was significantly related to OSA,  $F(4, 232)=5.34$ ,  $p < 0.05$ . Follow-up ANOVAs demonstrated that age  $F(1,236)=6.33$ ,  $p < 0.05$ , MS,  $F(1,236)=17.12$ ,  $p < 0.05$  and TMA,  $F(1,236)=5.27$ ,  $p < 0.05$ , distinguished between OSA patients and Normals. The follow-up comparisons revealed that patients with OSA compared with normals were older ( $M=50.04$  vs  $46.07$ ); had higher MS ( $M=3.79$  vs  $3.46$ ); and had larger TMA ( $M=161.33$  vs  $156.08$ ).

**AHI  $\geq$  30**

In this ANCOVA, 88 patients had OSA and 151 were Normal. The set of dependent variables was significantly related to OSA,  $F(4, 232)=5.50$ ,  $p < 0.05$ . Follow-up ANOVAs demonstrated that age,  $F(1,236)=5.09$ ,  $p < 0.05$ , MS,  $F(1,236)=11.33$ ,  $p < 0.05$  and TMA,  $F(1,236)=4.13$ ,  $p < 0.05$ , distinguished between OSA patients and Normals. The post hoc

comparisons revealed that patients with OSA compared with Normals were older ( $\underline{M}$ =50.75 vs 47.10); had higher MS ( $\underline{M}$ =3.84 vs 3.55); and had larger TMA ( $\underline{M}$ =163.88 vs 156.60).

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