Computed tomographic evaluation of the role of craniofacial and upper airway morphology in obstructive sleep apnea in Chinese

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Summary

Objectives: To evaluate the relationship between cephalometric parameters, upper airway morphological factors and obstructive sleep apnea (OSA) in Chinese subjects.

Design: Polysomnogram (PSG) were performed and scored using standard criteria. Supine lateral cephalometric parameters and pharyngeal cross-sectional areas at the level of velopharynx (VA) and hypopharynx (HA) were measured from computed tomographic scans. The roles of these parameters and other anthropometric/demographic characteristics in OSA (apnea hypopnea index, AHI > 5) and their relationship with severity of OSA were explored by multiple logistic and multinomial regression analysis.

Results: Ninety-two subjects, ranging from normal (n = 36), mild/moderate OSA (n = 34) to severe OSA (n = 22), were evaluated. Compared with normal subjects, OSA subjects were heavier (body mass index 27 vs. 24 kg/m\textsuperscript{2}) and older (47 vs. 42 years of age); had smaller VA size and VA to HA ratio, lower positioned hyoid bone, longer and thicker soft palate, and more retruded mandible relative to maxilla. After controlling for body mass index and age, subjects with severe OSA (AHI > 30) had more retruded mandible relative to maxilla (odds ratio, OR 1.31, \textit{P} = 0.044) and longer soft palate (OR 1.16, \textit{P} = 0.01), while those with mild/moderate OSA had larger VA to HA ratio (OR 0.17, \textit{P} = 0.018).

Conclusions: Craniofacial factors and upper airway morphology contributed to severity of OSA in Chinese subjects. Having controlled for obesity, more retracted mandible was associated with more severe OSA.

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Introduction

Obstructive sleep apnea (OSA) is characterized by repetitive occlusion of the upper airway during sleep. It is generally accepted that closure of the
airway is caused by the normal loss of upper airway muscle tone during sleep superimposed on a degree of upper airway narrowing. Besides obesity, craniofacial abnormality and size of upper airway have been linked with the development of OSA. Using lateral cephalometry, usually performed in standing posture, OSA subjects have been shown to have posteriorly placed maxilla and mandible, enlarged tongue and soft palate, and inferiorly positioned hyoid bone. Since posture is an important determinant of cephalometric parameters and upper airway dimension, computed tomography (CT) and magnetic resonance imaging (MRI), which are performed in the supine posture, have been applied as better imaging tools for assessing the upper airway in sleep apnea. These techniques are also superior in the delineation of soft tissue and airway lumen. Using such imaging techniques, difference in pharyngeal size and some bony or soft-tissue craniofacial parameters between normal and OSA subjects have been reported, but most of the studies had relatively small sample size and analysis did not control for obesity.

Asian subjects with OSA in most reported series had lower body mass indices, while at the same time displaying severe OSA compared to their Caucasian counterparts. There was also a trend for a lower risk of OSA attributable to obesity in Chinese subjects. Hence it has been postulated that craniofacial factors have a relatively bigger contribution to severity of sleep disordered breathing in Chinese than in Caucasians.

This study was designed to evaluate the relationship between craniofacial factors, including upper airway morphology, and the severity of OSA in Chinese.

Study population and methods

Subjects

Subjects were recruited from the Sleep Clinic of the University Department of Medicine, Queen Mary Hospital from January 1998 to December 2000. Majority of the subjects were recruited from a community-based study on prevalence of OSA. Subjects attending polysomnogram (PSG) for the prevalence study were invited to undergo CT of upper airway as well. Subjects were also recruited from a study on the efficacy of oral appliance in the treatment of mild/moderate OSA in which CT of the upper airway was one of the required tests at baseline. All recruited subjects gave informed consent and underwent PSG and CT of the head and neck region. The study was approved by the Ethics committee, The University of Hong Kong.

Sleep studies

All subjects underwent overnight polysomnography at baseline (Alice 3 Diagnostics System; Respironics, Pennsylvania, USA) with documentation of sleep stages by electroencephalogram, electrooculography, and electromyography; respiratory movement by impedance plethysmography; airflow by thermistor; arterial oxygen saturation by pulse oximetry, snoring by tracheal microphone, and sleep position by position sensor. All sleep data and respiratory events were manually scored according to standard criteria. The average number of episodes of apnea and hypopnea per hour of sleep (the apnea–hypopnea index, AHI) was calculated as the summary measurement of sleep disordered breathing. OSA was defined as AHI ≥ 5. Apnea hypopnea index 5–30 represented mild/moderate OSA and AHI ≥ 30 represented severe OSA.

Computed tomography (CT)

CT of the head and neck region was done for measurement of cephalometric indices and cross-sectional area of the airway at the level of velopharynx (tip of uvula) and hypopharynx (floor of vallecula). CT was performed in the head neutral (midway between flexion and extension), supine position with the subjects awake using a Hi-speed Advantage scanner (General Electric Medical System Milwaukee, USA). A lateral view scannogram was taken first to determine the level of different bony marking. Axial views were then obtained from the level of the hard palate to the hypopharynx. The lower limit of the hypopharynx was defined by identification of the thyroid cartilage. Scans were obtained during quiet tidal breathing within five seconds. Cephalometric measurements were made on the lateral scout view using an electronic cursor at the CT station by the same radiologist (WP) blinded to the clinical status of the subjects. The reference points for analyzing craniofacial morphology was based on standard protocol, and six standard bony and soft-tissue measurements, most commonly reported to show changes in OSA, were obtained. The definitions of these measurements are shown in Fig. 1. Cross-sectional area of the upper airway was manually measured at the level.
Computed tomographic evaluation

of velopharynx (VA), and hypopharynx (HA) using electronic calipers by another radiologist (CO).

Statistical analysis

Descriptive statistics were used to summarize subject characteristics. Numerical results were expressed as the mean ± SD. t-Test was used for comparison of demographic and CT data between OSA and normal groups and one-way ANOVA was used for comparison among normal, mild/moderate OSA and severe OSA groups.

To determine the cephalometric and upper airway variables that were individually associated with development of OSA (AHI ≥5), stepwise multiple logistic regression was used with AHI <5/≥5 as the dependent variable. The corresponding set of independent variables included gender, age, obesity (BMI or neck circumference), and one of the cephalometric parameters (Fig. 1) or upper airway parameters: velopharyngeal area, VA; hypopharyngeal area, HA; velo- to hypopharyngeal area ratio, VA/HA. To delineate the relative roles of craniofacial characteristics and obesity in the determination of severity of OSA, multi-nominal logistic regression was used, with OSA status categorized by AHI as the dependent variable. The corresponding set of independent variables were age, BMI and one of the upper airway or cephalometric parameters that was found to be significant in the multiple logistic regression.

Correlation between cephalometric parameters and upper airway cross-sectional area were examined by Pearson correlation coefficient.

Statistical analysis was performed by SPSS for Windows software (Version 10.0.7). Two-tailed P-values of less than 0.05 were considered to indicate statistical significance.

Results

Ninety-two subjects (67 from prevalence study and 25 from oral appliance study) were recruited of whom 69 were men. 36 of the subjects (all from the community-based prevalence study) had no OSA, as defined by AHI ≥5. 60% of the subjects with AHI <5 were habitual snorers, while 30% of those with AHI <5 were habitual snorers. Subjects with sleep apnea were more obese (Body mass index, 27 ± 3.4 vs. 24.2 ± 3.2 kg/m2, P < 0.001) and older (46.4 ± 8.5 vs. 41.5 ± 6.4 years, P = 0.002). They also had longer MPH (18.4 ± 6.1 vs. 11.4 ± 5.2 mm, P < 0.001), PMU (39.3 ± 5.3 vs. 34.7 ± 5.5 mm, P < 0.001), and Max-SP (11.9 ± 1.9 vs. 10.9 ± 1.8 mm, P = 0.01) as well as a smaller velopharyngeal to hypopharyngeal ratio (0.5 ± 0.39 vs. 0.7 ± 0.46, P = 0.03). The differences in these parameters were also demonstrated over the range of increasing severity of sleep disordered breathing (Table 1).

Stepwise multiple logistic regression models using AHI <5/≥5 as the dependent variable, controlled for age and neck circumference identified the following factors as determinants of the presence of OSA: VA, VA/HA ratio, MPH, PMU and ANB (Table 2). When BMI replaced neck circumference as the index of obesity in the model, similar parameters emerged except VA and ANB (Table 2).

In the multi-nominal regression model, older age, higher body mass index, smaller VA and longer MPH were consistently associated with both mild/moderate and severe OSA. However, when controlled for age and BMI, ANB and PMU were only associated with severe OSA and not mild/moderate OSA while...
a bigger velopharynx to hypopharynx ratio was only associated with mild/moderate OSA (Table 3).

Correlation analysis between cephalometric parameters and upper airway size showed that MPH was positively correlated with hypopharyngeal area \( (r = 0.235, P = 0.026) \), and negatively correlated with velopharyngeal area \( (r = -0.242, P = 0.021) \) and VA/HA ratio \( (r = -0.325, P = 0.002) \).

### Discussion

The findings of this study suggested that for a similar degree of obesity, differences in craniofacial and upper airway morphology contribute to the severity of OSA in Chinese subjects. Many studies have studied the craniofacial anatomy in OSA using various imaging techniques. Although conventional cephalometry can be done in supine position, computed tomographic technique carries significant advantages over plain roentgenographic imaging as it allows better delineation of soft tissue and air, hence more accurate measurements for upper airway morphology. Using CT to assess the upper airway and cephalometry in the same subject also provide a unique opportunity to evaluate the relationship between these two groups of parameters.

The most commonly reported craniofacial characteristics of OSA included inferiorly positioned hyoid bone, posteriorly placed maxilla and mandible, enlarged tongue and soft palate, and smaller velopharyngeal cross-sectional area. Such features have been similarly reported in both Caucasian and Asian subjects. However, in the majority of the studies, OSA subjects had significantly higher BMI and larger neck size than normal subjects. Neck circumference, an index of local adiposity in the context of OSA, has been shown to

### Table 1

Sample characteristics of subjects \((N = 92)\) according to severity of obstructive sleep apnea.

<table>
<thead>
<tr>
<th>Demographic and PSG data</th>
<th>AHI &lt; 5</th>
<th>AHI 5-30</th>
<th>AHI ≥ 30</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>36</td>
<td>34</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.5 ± 6.4</td>
<td>45.8 ± 8.2</td>
<td>47.2 ± 9.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Body mass index (BMI, kg/m²)</td>
<td>24.2 ± 3.2</td>
<td>26.8 ± 3.5</td>
<td>27.4 ± 3.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>37 ± 2.8</td>
<td>38.9 ± 3.3</td>
<td>39.9 ± 2.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Apnea hypopnea index (AHI)</td>
<td>1.5 ± 1.3</td>
<td>15.7 ± 6.5</td>
<td>38.5 ± 6.5</td>
<td></td>
</tr>
</tbody>
</table>

### Upper airway parameters

- Velopharynx, VA (mm²) 204 ± 94
- Hypopharynx, HA (mm²) 346 ± 134
- Velopharynx/hypopharynx 0.7 ± 0.46

### Cephalometry data

- MPH (mm) 11.4 ± 5.2
- SNA (deg) 96.6 ± 4.6
- SNB (deg) 91.9 ± 4.7
- ANB (deg) 4.8 ± 2
- PMU (mm) 34.7 ± 5
- Max SP (mm) 10.9 ± 1.8

### Table 2

Upper airway or cephalometric parameters identified as independent determinants of OSA (defined by AHI < 5 or ≥ 5), controlled for age and neck circumference/BMI.

<table>
<thead>
<tr>
<th>Neck circumference</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>BMI</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>0.994</td>
<td>0.988-0.999</td>
<td>0.292</td>
<td>0.094-0.905</td>
<td></td>
</tr>
<tr>
<td>VA/HA</td>
<td>0.228</td>
<td>0.068-0.760</td>
<td>1.208</td>
<td>1.087-1.341</td>
<td></td>
</tr>
<tr>
<td>MPH</td>
<td>1.228</td>
<td>1.104-1.366</td>
<td>1.003-1.638</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANB</td>
<td>1.282</td>
<td>1.000-1.191</td>
<td>1.000-1.203</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMU</td>
<td>1.091</td>
<td>1.000-1.191</td>
<td>1.000-1.203</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI = confidence interval.

### Table 3

##
correlate with the size of the tongue, soft palate, position of maxilla, mandible and hyoid bone. Therefore, to compare cephalometric parameters and upper airway size without controlling for obesity would subject the results to confounding effects.

Obesity has been shown to be an important factor in the development as well as severity of OSA in Chinese subjects, and this was further confirmed in this study. A more receded mandible and/or maxilla relative to the nasion, reflected by smaller SNB and SNA, respectively, has been frequently cited as a contributing factor to severity of OSA. One Japanese study showed that OSA subjects had smaller SNA and SNB when compared with normal subjects but only subjects with severe OSA were studied. Our results showed that neither SNA nor SNB contributed to the severity of OSA, but the discrepancy between the maxilla and the mandible as reflected by a bigger ANB, was an independent determinant of severe OSA. In a previous study, Chinese subjects with severe OSA had been shown to have smaller SNB and cross-sectional area at the level of velopharynx and hypopharynx compared with age and BMI matched controls. Although the imaging technique used was the same as the current study, the numbers of OSA subjects were smaller and not all normal subjects had PSG confirmation.

When matched for age and BMI, Far-East Asian men have been found to have more severe OSA than that of Caucasian counterparts. Chinese subjects were also found to have more severe craniofacial skeletal discrepancies than Caucasian counterparts when matched for age, gender, BMI and AHI. However, it is now established that the BMI criteria for obesity in Asian are lower than Caucasians, and matching for obesity between subjects of different ethnicity using numerically similar BMI is probably not valid. Nonetheless, the risk of developing OSA attributed to increments in obesity indices was probably lower compared to Caucasians. Previous studies in Japanese and Caucasians have also reported that cephalometric features were more important risk factors for OSA in non-obese compared to obese subjects. Our findings thus lend further support that craniofacial factors, in particular a more receded mandible relative to the maxilla may be one of the factors that predispose Chinese to develop more severe OSA at a lower degree of obesity compared to Caucasians.

The hyoid bone serves as anchorage for the tongue muscles and inferiorly positioned hyoid bone in OSA is well documented. It has been postulated that accumulation of adipose tissue in the submental and submandibular region pushed the hyoid bone more inferiorly. Others suggested that inferiorly placed hyoid bone relocate the tongue base into hypopharynx thus the patency of the hypopharyngeal airway is adversely affected. We found that after controlling for neck circumference, a surrogate marker for neck adiposity, the position of the hyoid bone remained an independent risk factor for the development of OSA. The negative correlation between mandibular plane-hyoid bone distance and velopharyngeal level and hence predispose to upper airway collapse.

A long and thick soft palate is commonly seen in OSA subjects. In this study, length of soft palate was recorded using computed tomographic evaluation.

### Table 3: Multi-nominal logistic regression models for different groups according to severity of OSA.

<table>
<thead>
<tr>
<th>Disease severity</th>
<th>P-value</th>
<th>Odds Ratio 95%CI Lower Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA/HA Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.004</td>
<td>1.13 1.04 1.22</td>
</tr>
<tr>
<td>BMI**</td>
<td>0.001</td>
<td>1.39 1.14 1.69</td>
</tr>
<tr>
<td>VA/HA</td>
<td>0.292</td>
<td>0.5 0.14 1.82</td>
</tr>
<tr>
<td>Mild/moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>0.014</td>
<td>1.10 1.02 1.18</td>
</tr>
<tr>
<td>BMI**</td>
<td>0.003</td>
<td>1.31 1.10 1.57</td>
</tr>
<tr>
<td>VA/HA*</td>
<td>0.018</td>
<td>0.17 0.04 0.74</td>
</tr>
<tr>
<td>ANB Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>0.006</td>
<td>1.12 1.03 1.22</td>
</tr>
<tr>
<td>BMI**</td>
<td>0.001</td>
<td>1.43 1.16 1.75</td>
</tr>
<tr>
<td>ANB*</td>
<td>0.044</td>
<td>1.31 1.01 1.70</td>
</tr>
<tr>
<td>Mild/moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>0.034</td>
<td>1.08 1.01 1.16</td>
</tr>
<tr>
<td>BMI**</td>
<td>0.001</td>
<td>1.35 1.13 1.61</td>
</tr>
<tr>
<td>ANB</td>
<td>0.218</td>
<td>1.16 0.92 1.48</td>
</tr>
<tr>
<td>PMU Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>0.010</td>
<td>1.12 1.03 1.22</td>
</tr>
<tr>
<td>BMI</td>
<td>0.005</td>
<td>1.34 1.09 1.65</td>
</tr>
<tr>
<td>PMU*</td>
<td>0.010</td>
<td>1.16 1.04 1.29</td>
</tr>
<tr>
<td>Mild/moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>0.042</td>
<td>1.08 1.00 1.59</td>
</tr>
<tr>
<td>BMI</td>
<td>0.003</td>
<td>1.30 1.09 1.56</td>
</tr>
<tr>
<td>PMU</td>
<td>0.133</td>
<td>1.07 0.98 1.18</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.005; ***P<0.001.
palate correlated positively with AHI, and it was a significant factor only in subjects with severe OSA but not in mild/moderate OSA, when obesity and age were held constant. Although a long and thick soft palate may theoretically result in a crowded pharynx and contribute to more severe sleep apnea, such abnormalities may also be the result of greater traumatic soft tissue edema induced by recurrent apneic episodes in severe OSA.\textsuperscript{33} Our study design could not further clarify this relationship.

The velopharynx is the most collapsible part of the upper airway, and it has been repeatedly reported to be smaller in OSA subjects.\textsuperscript{34-36} After controlling for confounding factors such as age and obesity, we confirmed that cross-sectional area of velopharynx was a significant determinant of the presence of OSA. Furthermore, we found that a smaller velopharynx to hypopharynx ratio was associated with a higher AHI. A previous study also reported that OSA subjects had narrower velopharynx and smaller velopharynx to hypopharynx ratio than normal subjects, although the analysis did not control for potential confounding factors of obesity and age. Based on their findings, the workers postulated that a smaller hypopharynx could protect against upper airway collapse because peak inspiratory pressure was damped at this level, resulting in a lower suction force on the more collapsible velopharynx upstream.\textsuperscript{7} The corollary of this theory was that airway collapse was favored by a narrow velopharynx associated with a large hypopharynx and our findings support this postulation.

It must be emphasized that the imaging of the upper airway was conducted while the subject was awake and during quiet tidal breathing. It is known that airway dimensions can vary during the breathing cycle,\textsuperscript{37} therefore it might have been better to ask the subjects to hold their breath at end expiration, although this would still not have reflect the "true" dimensions of the airway during sleep. Airway volume has not been measured and therefore we cannot comment on the difference in upper airway volume between normal and OSA subjects. However, in a recent study, CT of the upper airway did not show any difference in upper airway volume between OSA subjects and snorers.\textsuperscript{36}

**Conclusion**

In summary, our findings demonstrated that having controlled for obesity, inferiorly positioned hyoid bone, longer soft palate, smaller velo- to hypopharynx ratio and a mandible more posteriorly positioned relative to the maxilla were independently associated with OSA. In particular, relative reposition of the mandible was independently associated with severe OSA in Chinese.

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**References**


