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ORIGINAL ARTICLE

Craniofacial obesity in patients with obstructive sleep apnea

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Abstract
Introduction Obstructive sleep apnea (OSA) and obesity are serious, widespread public health issues.
Objective To localize and quantify geometric morphometric differences in facial soft tissue morphology in adults with and without OSA.
Materials and methods Eighty adult Malays, consisting of 40 patients with OSA and 40 non-OSA controls, were studied. Both groups were evaluated by the attending physician and through ambulatory sleep studies. 3-D stereophotogrammetry was used to capture facial soft tissues of both groups. The 3-D mean OSA and control facial configurations were computed and subjected to principal components analysis (PCA) and finite-element morphometry (FEM).
Results The body mass index was significantly greater for the OSA group (32.3 kg/m^2 compared to 24.8 kg/m^2, $p<0.001$). The neck circumference was greater for the OSA group (42.7 cm compared to 37.1 cm, $p<0.001$). Using PCA, significant differences were found in facial shape between the two groups using the first two principal components, which accounted for 50% of the total shape change ($p<0.05$). Using FEM, these differences were localized in the bucco-submandibular regions of the face predominantly, indicating an increase in volume of 7–22% ($p<0.05$) for the OSA group.
Conclusion Craniofacial obesity in the bucco-submandibular regions is associated with OSA and may provide valuable screening information for the identification of patients with undiagnosed OSA.

Keywords Facial soft tissues · Adult · Sleep apnea · Morphometrics · Obesity · Asian

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Introduction

Obstructive sleep apnea (OSA) and obesity have been described as serious public health problems. Despite this claim, OSA is still widely unidentified and undiagnosed. The failure to recognize OSA is in part due to the limited availability of diagnostic facilities and to the non-specific nature of symptoms associated with OSA [1], which can have other possible causes [2]. On the other hand, the diagnosis of OSA is considered to be important because it increases the risk of hypertension, cardiac arrhythmias, and mortality. For example, undiagnosed OSA has been found in 15–39% of patients with hypertension, 35% of patients with congestive heart failure, and 13% of patients with coronary artery disease [3]. Thus, failure to recognize OSA is costly both to the individual and to the society; underdiagnosis is thought to cost the USA $3.4 billion in additional medical costs per year [4]. Therefore, various attempts have been made to identify patients with OSA using diagnostic algorithms based on features of history, physical examination, overnight oximetry, clinical [5] and morphometric prediction models [6], but with limited success [1].

Currently, OSA is diagnosed through history-taking, clinical and physical examination, polysomnography, and

imaging studies. Imaging techniques that have been extensively used include 2-D lateral cephalometric radiography. Several cephalometric differences between Asian (Chinese) patients with OSA and control samples have been reported. These differences include mandibular deficiency, bimaxillary retrusion, shortened cranial base, reduced cranial base angle, reduced mandibular length, increased lower anterior facial height, altered craniocervical angulation, an inferiorly positioned hyoid bone, and enlargement of the soft palate [7]. In addition, early studies of OSA emphasized the importance of obesity as a significant determinant of sleep-disordered breathing (SDB). For example, the Wisconsin Sleep Study reported that obesity increases the risk of OSA in adults of both sexes [8]. As well, obesity and a dolicocephalic facial pattern were identified as the most significant risk factors in Japanese men [9] with OSA, and obesity was significantly correlated with the severity of OSA [10].

On the other hand, few studies on OSA have used 3-D imaging with geometric morphometric methods, such as finite element morphometry (FEM). Using FEM, the change in morphology is viewed as a deformation of an initial geometric configuration, whose boundaries are formed by edges that connect anatomical landmarks, into a final form [11]. Indeed, this technique has been employed previously in studies of craniofacial growth [12], facial soft tissue changes [13–15], and dental arch features [16]. Thus, it is thought that FEM allows a better understanding and visualization of the magnitude and direction of morphologic change [17]. For example, thin-plate spline analysis was used to investigate the 2-D shape characteristics of the face and tongue in patients with OSA. It was found that major shape changes in patients with OSA were located mainly in the lower part of the face and in the upper part of the neck [18]. In addition, the 2-D characteristics of the cranial base and upper airway morphology in patients with OSA were also investigated using FEM. It was found that functional airway impairments were associated with size reduction in the posterior cranial base [19]. Nevertheless, published literature regarding soft tissue facial morphology and its association with OSA is minimal, especially in comparison with the numerous articles that can be found concerning skeletal changes that are found in patients with OSA. Therefore, the aim of this study is to determine 3-D differences in the facial soft tissue morphology of adult Malays with and without OSA. This study will test the null hypothesis that no 3-D morphologic differences in terms of facial size and shape are identifiable in patients with OSA when compared to a matched control group of non-OSA volunteers.

Materials and methods

This multidisciplinary study took place in the Clinic of Otorhinolaryngology–Head and Neck Surgery (ORL-HNS), Hospital Universiti Sains Malaysia (HUSM). A comparative, cross-sectional study design was employed. Exclusion criteria for sample selection were any subjects with psychiatric illness, sedative and/or alcohol intake, patient-specific disorders (such as neuromuscular disorders), any craniofacial deformity (such as cleft lip and/or palate), and lack of informed consent or willingness to participate in the study. After obtaining informed consent, which was reviewed and approved, 80 adult Malays aged 18–60 years were recruited for this study. The first group consisted of 40 consecutive, care-seeking, snoring patients with OSA [defined as an Apnea-Hypopnea Index (AHI) >5/h of sleep] diagnosed with ambulatory sleep studies. The second group consisted of 40 consecutive, healthy, non-OSA control subjects who did not have any apneic symptoms, including snoring, as evaluated by the attending physician and ambulatory sleep studies. The main sources of both groups included in the study were randomly selected subjects from the ORL-HNS and the Orthodontic clinic. In addition, individual nurses, medical/dental students, and university staff were also asked to seek volunteers for the study. Each patient's age, sex, height, and weight were recorded. The body mass index (BMI) was calculated from the patient's height and weight in standard units (kg/m^2), and the neck circumference (NC) was measured at the level of the thyroid cartilage.

An overnight hospital type III sleep study was performed on each subject between 2200 to 0600 hours. All variables were recorded simultaneously and continuously with a portable diagnostic device (Embletta, Somnologica, Iceland) at HUSM Sleep Science Laboratory. This device has been reported to be suitable for use both in hospitals and at home [20] and has been validated against full polysomnography [21]. The parameters measured were as follows: nasal airflow, using two appropriately placed thermistors; thoraco-abdominal movements, via two piezo-electric bands; pulse oximetry, using a finger probe; snoring episodes, detected via a vibration sensor placed anterior to the sternomastoid muscle; and continuous actigraphy, to monitor and record body position. Outputs from the portable diagnostic device were scored automatically and manually (if there was any uncertainty) by two sleep laboratory technicians who had no prior knowledge of the clinical characteristics of the subject. Using the automatically scored data, the AHI (events per hour) was computed using a software program (Somnologica; Flaga Medical Devices). Occurrence of OSA was scored when there was cessation of breathing for >10 s associated with evidence of persistent respiratory effort. Hypopnea was scored when there was >50% decrease in the airflow signal with >3% decrease in arterial oxygen saturation [22]. Therefore, the severity of OSA was evaluated by the AHI, defined as the total number of apneas and hypopneas divided by the total sleep time in minutes. Central and obstructive apneas were distinguished by the presence or absence of thoraco-abdominal movements

during an apnea. The AHI was calculated as the number of respiratory events per hour of recording time in bed, with the start of recording being the point at which respiration settled to a rhythmic, stable pattern. The end of the recording time was either the waking time recorded by the subject or the point at which the thoraco-abdominal tracings became disturbed, which was consistent with wakefulness. At the end of the study, individual results were communicated to each patient and, where appropriate, treatment was offered. For the OSA group, patients with mild OSA had an AHI of 5–15/h. Patients with moderate OSA had an AHI of 15–30/h, and patients with severe OSA had an AHI >30/h. The control group included subjects whose AHI ranged from 0–4/h [22].

After receiving all subjects' sleep reports, a 3-D stereophotogrammetry unit (3dMD, Atlanta, GA, USA) was used to capture the 3-D facial soft tissues using a standardized protocol. The 3dMD system is a combination of hardware and software that together produces 3-D images of patients. Once aligned, the patient was seated upright at a distance of 175 cm in front of four camera pods, each consisting of two geometry cameras, one texture camera, a white light flash, and a speckle flash. The 3dMD system captured the images in <2 ms. The images were then processed to give a 3-D surface image. From the 3-D stereophotogrammetry images, nine homologous facial soft tissue landmarks (Fig. 1) were digitized using MorphoStudio software to obtain the x, y, z coordinates. The researcher (SMB) first digitized all images regardless of which group they belonged to; only during analysis were both groups separated. As well, all data were subjected to duplicate digitization by the same investigator on two different occasions. Next, the mean 3-D facial morphologies were determined for both groups using more than 1,553 vertices per patient (Fig. 2). Thus, although initially only nine landmarks were manually digitized, the remaining 1,542 were computed using dense correspondence so that all regions of the face could be analyzed [23]. For statistical testing, principal components analysis (PCA) was used to identify significant shape changes, and FEM was used to compare the mean 3-D OSA facial morphology with the mean 3-D control facial morphology. These methodologies have been described in detail elsewhere [24–27] and will not be repeated in this paper. In addition, MorphoStudio software was used to perform an inter-landmark analysis. This analysis detects statistical changes in length of linear distances between landmarks in the mean 3-D facial morphologies.

Results

On duplicate digitization of the landmarks, no significant differences were found ($p>0.05$) using a method equivalent to Dahlberg's formula, and therefore, the study digitization error was assumed to have no effect on the findings. In the current study, the BMI was found to be significantly greater for the OSA group (32.3 kg/m^2±7.4) when compared to the control group (24.8 kg/m^2±6.5, $p<0.001$). In addition, the neck circumference was greater for the OSA group (42.7 cm±2.5) compared to the control group (37.1 cm±2.2, $p<0.001$). The AHI was also significantly greater for the OSA group (40.0/h±30.3) when compared to the control group (2.0/h±2.0, $p<0.001$). As well, the lowest oxygen saturation was significantly lower for the OSA group (76.4%±11.4) compared to the control group (86.9%±9.4, $p<0.001$). These variables are summarized in Table 1.

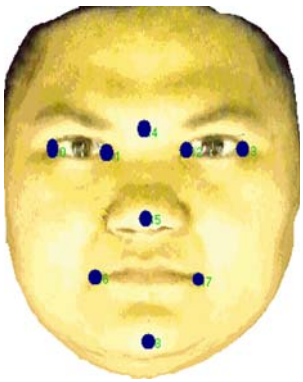

Fig. 1 Definitions of manually digitized homologous facial soft tissue landmarks. *0* Right lateral canthus, *1* right medial canthus, *2* left medial canthus, *3* left lateral canthus, *4* soft tissue nasion, *5* pronasale, *6* right oral commisure, *7* left oral commisure, *8* soft tissue pogonion

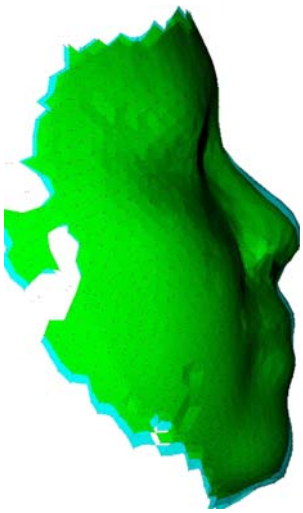

Fig. 2 The mean 3-D OSA facial morphology (*blue*) superimposed on the mean 3-D control facial morphology (*green*). Note that the mean 3-D OSA facial morphology appears to be larger in volume in the submandibular region as well as in the upper lip and nasal regions

Table 1 Sample characteristics assessed in this study

		Mean	Std. Deviation	Significance
Apnea-hypopnea index (events/hr)	Control	2.00	2.02	$P<0.001$
	OSA	40.04	30.31	
Average oxygen saturation (%)	Control	97.18	3.90	$P<0.001$
	OSA	94.72	3.32	
Lowest oxygen saturation (%)	Control	86.89	9.36	$P<0.001$
	OSA	76.35	11.44	
Body mass index (kg/m^2)	Control	24.79	6.46	$P<0.001$
	OSA	32.29	7.40	
Neck size (cm)	Control	37.1	2.16	$P<0.001$
	OSA	42.7	2.52	

OSA Patients with obstructive sleep apnea

Using PCA (Fig. 3), significant differences were found between the OSA and control groups using the first two eigenvalues, which accounted for >49% of the total shape change ($p<0.05$). Using FEM, these differences were localized in the bucco-submandibular regions of the face predominantly (Fig. 4), with the OSA inter-landmark distances (Fig. 5) indicating an increase in volume of 7–22% ($p<0.05$).

Discussion

In this current study, the differences in 3-D facial morphology in adult Malays with and without OSA were investigated using landmark-based finite-element analysis (FEM) to localize and quantify any differences. Although facial measurements from photographs using instruments, such as rulers or calipers, have been deployed both in 2-D and 3-D, the advantages of measurements using 3-D photogrammetry over direct surface measurements are recognized. For example, the period of communication with the subject is potentially shorter, and the technique is less dependent on patient behavior [28]. In addition, direct surface measurements may deform the facial surface and lead to inaccuracies [29]. Therefore, soft tissue landmarks measurements are thought to be more suited to photogrammetry, while direct measurements are preferable for bony landmarks that require palpation [28]. Despite the above contention, the current study could not overcome some methodological limitations. First, the sample size was relatively small, limited by the number of subjects that met the criteria of the study. Second, generalization of the results

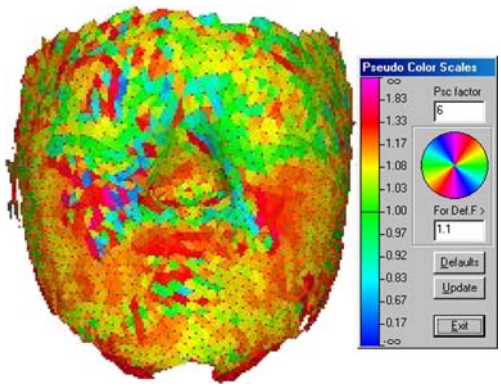

Fig. 4 Pseudo-colored finite-element analysis, comparing the mean 3-D facial morphology of patients with OSA with the mean 3-D facial morphology of control subjects. The *vertical pseudo-color scale* indicates that the differences are localized in the buccosubmandibular regions of the face predominantly (*red-orange*)

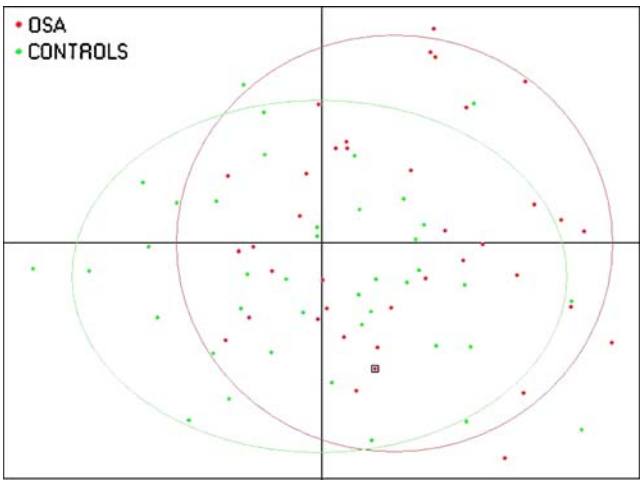

Fig. 3 Principal components analysis comparing 3-D facial morphology of patients with OSA (*red dots*) with control subjects (*green dots*). Using the first two principal components, which account for >49% of the total shape change, a significant difference was detected ($p=0.026$)

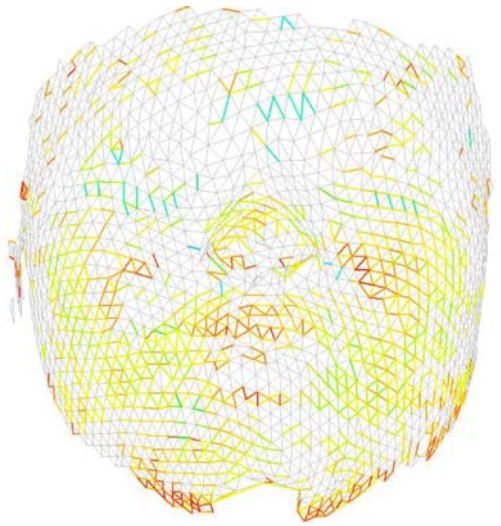

Fig. 5 Pseudo-colored inter-landmark analysis indicating statistically significant changes in 3-D distances ($p<0.05$). An increase in volume of 7–22% is indicated by the *red-orange lines*

to a larger population is limited because the sample subjects were care-seeking volunteers at a hospital clinic. This source of study subjects could introduce a potential selection bias into the investigation and make our results more applicable to hospital populations rather than the general public. Third, this study used 3-D facial soft tissue of patients with OSA during wakefulness. Nevertheless, abnormalities of upper airway anatomy and physiology in subjects with OSA during wakefulness have been clearly documented [30]. Therefore, we believe that careful assessment of OSA data during wakefulness may provide some valuable information, even though decision rules may provide an alternative to polysomnography in the diagnosis of OSA [31]. Finally, generalization of the present results to different ethnicities, including other Asian populations, is limited because ethnic Malays may have unique craniofacial features.

In the current study, there were demonstrable differences in the facial soft tissues, which were mainly localized in the bucco-submandibular regions using FEM (Fig. 4). In support of this finding, the inter-landmark distances of the Procrustes means [26] (Fig. 5) indicated an increase in soft tissue facial size of 7–22% in the OSA group compared with the control group. Although little attention has been given to examination of the facial soft tissues in the diagnostic assessment of OSA, it has been reported that analysis of soft tissues covering the underlying skeletal framework allows a more comprehensive assessment of obese subjects [32]. In addition, the significance of antero-posterior dimensions of the face in obese patients with SDB has been consistently reported in Caucasian populations [33]. In this current study, we used FEM, a relatively new analytic tool, to depict the facial soft tissue alterations in Malays. However, most previous studies have compared patients with OSA to controls using conventional techniques [1, 7]. In a previous study using FEM in Malay patients with OSA, it was found that posterior cranial base morphology was associated with airway impairment [19]. Thus, although the FEM method appears to be somewhat constructed, one advantage is that the results are presented graphically and one can view changes in size or shape. In addition, it has been found that the major form changes in patients with OSA are found mainly in the lower part of the face and upper part of the neck using thin plate splines [18], which is in good agreement with our current study. Furthermore, we were able to localize those changes and quantify them using 3-D FEM.

Increased fat deposition as a submandibular pannus, which is suggested by the present study may be one of the factors that makes patients more prone to severe forms of sleep apnea. The submandibular region does not have a bony structure, thereby permitting accumulation and expansion of excessive soft tissues, both internally and externally. This accumulation may lead to displacement of the hyoid bone inferiorly and an increase in submandibular area, as reported previously [19]. Consequently, the inferiorly placed hyoid bone may relocate the tongue base into the hypopharynx, and thus, the patency of the hypopharyngeal airway may be adversely affected [34]. While most previous studies report the significance of skeletal craniofacial factors as major risk factors that may result in narrowing the upper airway in Asians [1, 35], according to the current findings, changes in the overlying facial soft tissue may also indicate effects on the airway of patients with OSA. Furthermore, it has been reported that a certain bony framework of the upper airway leads to a particular layering of soft tissues onto that framework, which in turn provides an integrated anatomical configuration that affects the maintenance of upper airway patency during sleep [36]. We therefore suggest that excessive soft tissues (both internally and externally) allied with a reduction in size of the cranial base may cause displacement of the hyoid bone in this group of patients. Accordingly, both obesity and craniofacial abnormalities may synergistically increase the tissue pressure surrounding the pharynx and therefore increase the closing pressure of the passive pharynx in patients with SDB [37,38].

In view of the above contention, it would be reasonable to hypothesize that craniofacial obesity can significantly impact airway collapsibility and may, in part, explain the predisposition of adult Malays to OSA. Therefore, a combination of factors, which includes craniofacial and oropharyngeal anatomic abnormalities, as well as the size of the patient, might be more predictive of OSA than any single factor alone [39]. In summary, this study suggests that there are clearly definable differences in facial soft tissues when comparing patients with OSA to control subjects, with obesity acting as an additional risk factor in this particular group of Asian patients. Furthermore, on the basis of computational FEM modeling, we believe that craniofacial obesity appears to be a feature associated with OSA, and may provide valuable screening information in the identification of patients with undiagnosed OSA.

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