Abstract

Objective  Many Japanese patients with obstructive sleep apnea (OSA) are less obese than Caucasian OSA patients despite their similar severity of OSA, suggesting that their etiology of OSA may differ. The purpose of this study was to identify bony factors associated with OSA in the Japanese population.

Methods  The clinical records of study subjects were retrospectively reviewed, and cephalometric measurements based on Sella-Nasion references and the Ricketts method were statistically compared.

Patients  Two hundred and six consecutive Japanese men complaining of habitual snoring and daytime sleepiness were enrolled in the study. All subsequently underwent an overnight polysomnographic examination.

Results  Multiple regression analysis showed that the body mass index (p<0.0001) and facial axis angle (p=0.007) were the dominant overall determinants for the apnea hypopnea index. The sella to nasion to subspinale angle (SNA) and sella to nasion to supramentale angle (SNB) were lower in the non-obese, severe group than for non-obese, mild and moderate patients with OSA (p=0.0047 and 0.0016, respectively).

Conclusion  The risk factors for OSA in Japanese men may be obesity and the dolico facial pattern seen by the Ricketts method. In addition, a smaller SNA and SNB seem to be associated with the severity of OSA in non-obese patients.

(Internal Medicine 44: 805–810, 2005)

Key words: sleep disordered breathing, cephalometrics, facial axis angle

Facial Axis Angle as a Risk Factor for Obstructive Sleep Apnea

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Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive upper-airway collapse during sleep. The patency of the human upper-airway is mostly maintained by muscle activation and soft tissue structures. Variables that promote pharyngeal collapse include negative pressure within the airway (e.g., during inspiration) and positive pressure outside the airway such as fat deposition and from having a small mandible (1). In addition to muscle activation and soft tissue structures, skeletal factors are also the major determinants of upper-airway patency during sleep (2). Patients of normal body weight in whom OSA develops may have tonsillar hypertrophy or craniofacial skeletal abnormalities that also predispose the airway to narrowing or closure during sleep (3). Cephalometric radiographs were among the earliest techniques used to image the upper-airway and revealed that patients with OSA have a reduction in the length of the mandible, an inferiorly positioned hyoid bone, and retroposition of the maxilla (4). Most studies involving cephalometric analyses of patients with OSA have been based on a Sella-Nasion reference. Many Japanese patients with OSA are less obese despite the similar severity of OSA compared with Caucasian OSA patients (5). Fundamental variations exist between the craniofacial structure of Japanese and Caucasians. An investigation that compared the lateral cephalograms of untreated Japanese and European-Americans with normal occlusions and well-balanced faces revealed that Japanese, in general, have smaller anteroposterior facial dimensions and proportionately larger vertical facial dimensions(6). The Ricketts method uses three vertical measurements: the facial axis, lower facial height, and total facial height, and the facial patterns of Japanese
OSA patients are dolico (long face) classified by the Ricketts method (7).

The purpose of this study was to investigate the cephalometric risk factors for the development of OSA in the Japanese population using Sella-Nasion references and the Ricketts method on large sample groups. The relationships between the cephalometric parameters and apnea severity in non-obese and obese patients with OSA were also evaluated.

Materials and methods

Subjects

We reviewed the charts and cephalograms of 206 consecutive Japanese men, who were referred to Niigata University Medical and Dental Hospital and Niigata Rinko Hospital between December 1999 and November 2003, complaining of habitual snoring and daytime sleepiness. All subsequently underwent an overnight polysomnographic study (PSG). We excluded patients with renal failure, thyroid dysfunction, and psychiatric disorders. All the subjects gave their written informed consent to participate in this project.

Polysomnography

PSG (Somnostar; SensorMedics, Yorba Linda, CA) was carried out including electroencephalography (EEG), electromyography (EMG), electrooculography (EOG), electrocardiography (ECG), examination of airflow using an oronasal thermistor, along with the measurement of chest and abdominal wall movements, oxygen saturation using a pulse oximeter, snoring sounds using a tracheal microphone, and body position. The data was scored according to standard criteria. Also, the severity of sleep apnea was assessed by the average number of apnea plus hypopnea per hour of sleep [apnea-hypopnea index (AHI)], the lowest oxygen saturation (lowest SpO2), the cumulative percentage of sleep time with oxygen saturation below 90% (CT90%), and the average number of arousals per hour of sleep [arousal index (ArI)].

Cephalometry

A lateral cephalogram without swallowing for each subject was obtained in the sitting position during the end-expiratory phase. A cephalostat was used to keep the subject's head in a position such that the Frankfurt horizontal line was parallel to the floor during exposure. The cephalometric landmarks and reference lines are shown in Fig. 1. The following angles and dimensions were measured: SNA; the angle formed by lines connecting S, N, and A, SNB; the angle formed by S, N, and B, NSBa; the angle formed by N, S, and Ba, and facial axis angle (FX); the angle formed by Ba, CC, and Gn.

Statistical analysis

The BMDP Statistical Package program (BMDP; Los Angeles, CA) was used for multivariate adjustments for all covariates, simultaneously, using Cox regression analysis. Comparison of the PSG data and cephalometric measurements between the groups was performed using the Mann-Whitney U test with Statview V (Abacus Concepts, Berkeley, CA). A p-value of less than 0.05 was considered to indicate statistical significance.

Results

The PSG data and cephalometric measurements of all subjects are presented in Table 1. Seventeen cases were simple snorers because they had less than five episodes of apnea and hypopnea per hour during overnight PSG, while the other 189 patients were diagnosed with OSA. Multivariate analysis using Cox regression analysis on AHI was made with regard to age, BMI, and four cephalometric variables: SNA, SNB, NSBa, and FX, and independent factors for AHI were found to be BMI (p<0.0001) and FX (p=0.007). The other factors of age, SNA, SNB, and NSBa were not included as predictive variables (Table 2).

One hundred and eighty-nine patients with OSA were then divided into four groups based on their BMI and AHI: a non-obese, mild and moderate group with BMI <27 and 5< = AHI <30; a non-obese, severe group with BMI <27 and 30< = AHI; an obese, mild and moderate group with 27< = BMI and 5< = AHI <30; and an obese, severe group with 27< = BMI and 30< = AHI. Cephalometric parameters were compared between the non-obese, mild and moderate group and the non-obese, severe group (Table 3), and no difference was found in the age or BMI between the two groups. SNA and SNB were lower in the non-obese, severe group, but FX was not
The mean±SD are shown. PSG: polysomnographic study, BMI: body mass index, AHI: apnea hypopnea index, lowest SpO₂: lowest oxygen saturation, CT90%: cumulative percentage of sleep time with oxygen saturation below 90%, ArI: arousal index.

Table 2. Multiple Regression Model on AHI for All Subjects

<table>
<thead>
<tr>
<th>Factors</th>
<th>Coefficient</th>
<th>SE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>12.188</td>
<td>1.839</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FX, degree</td>
<td>-6.214</td>
<td>1.737</td>
<td>0.007</td>
</tr>
</tbody>
</table>


FX as a Risk Factor for Japanese OSA

different between the groups. A comparison of cephalometric parameters did not show any differences between the mild and moderate group and the severe group in obese patients with OSA (Table 4). We also compared the data for the non-obese, mild and moderate group with those of the obese, mild and moderate group. There were no differences in age, AHI, CT90%, lowest SpO₂ and cephalometric variables between the two groups, and only ArI was slightly greater in the non-obese, mild and moderate group (p<0.05) in addition to the BMI. When we compared the non-obese, severe group to the obese, severe group, the age and lowest SpO₂ were higher (p<0.01), the AHI (p<0.05) and CT90% (p<0.01) were lower, and the SNA (p<0.01), SNB (p<0.01) and FX (p<0.05) were smaller in the non-obese, severe group. We finally compared the cephalometric data between the age-matched non-obese, severe group and obese, mild and moderate group (Table 5). The SNB and FX were lower in the non-obese, severe group, but the SNA and NSBa were not different.
Discussion

The present study examined four cephalometric variables in 206 Japanese men complaining of habitual snoring and daytime sleepiness. We found that the FX was included as one of the predictive variables of OSA in a multiple regression model for the overall subjects. Comparison of the cephalometric parameters by univariate analyses indicated that the SNA and SNB were different between the mild and moderate group and the severe group in non-obese patients with OSA, but that the FX was not different. These results suggest that the FX may be a factor for being susceptible to OSA in addition to the BMI in Japanese men, and that the severity of OSA may depend on the SNA and SNB only in non-obese patients.

Narrowing of the pharyngeal airway as a result of alterations in craniofacial morphology has been suggested in the etiology of OSA. Also, alterations in the maxillomandibular complex and microgrowth or retrognathism of the jaws may be of significance in the pathogenesis of upper pharyngeal airway narrowing in OSA (8), and a more inferiorly positioned hyoid bone (9), larger gonial angle (10), smaller anterior cranial base (11), and altered anterior and posterior facial heights are significant (11). Reports on observed alterations in craniofacial morphology, however, are inconsistent (12). A recent cephalometric analysis of 31 Caucasian male patients with OSA and 37 healthy Caucasian subjects with multiple regression models revealed that the hyoid bone position is of predictive value in the cephalometric discrimination between OSA and non-OSA subjects (13). Also, a cephalometric analysis of 73 men with OSA performed in the UK showed that the skeletal craniofacial structure is similar in obese and non-obese subjects (14).

The comparison of Far-East Asian men with Caucasian men revealed that Asian men have more severe OSA despite being less obese, suggesting that the etiology of sleep disordered breathing in Asians may differ from that of Caucasians (5). Two bony structure variables, the anterior cranial base length, the distance between S and N, and the mandibular length, the distance between Me and the Go (gonion, a midplane point at the gonial angle located by bisecting the posterior and inferior borders of the mandible) are significant in a stepwise regression model of AHI for non-obese Japanese patients with OSA (15). A cephalometric study that used a small sample size showed that the SNA, SNB, NSBa, MP-H, the distance from the mandibular plane to the hyoid bone, and the PNS-P, the distance from the posterior nasal spine to the tip of the soft palate indicating the length of the soft palate, are significantly different between non-obese patients with OSA and normal Japanese controls (16). A recent systematic study of 62 male Japanese patients with OSA and 13 male snorers with AHI less than five events per hour showed that obese and non-obese patients with OSA show significant cephalometric features compared with simple snorers including an inferiorly positioned hyoid bone, enlarged soft palate, and reduced upper airway width at soft palate, but that the SNA, SNB, and NSBa are not different (17).

Lateral cephalometric norms may be specific to an ethnic group and cannot always be applied to other ethnic types. The comparison of craniofacial structures between 44 European-American men and 26 Japanese men indicated that the Japanese sample for lateral cephalometric radiographs is smaller in terms of anteroposterior facial dimensions and proportionately larger in terms of vertical facial dimensions (6). Also, the FX is smaller in Japanese subjects, indicating a more downward direction of facial development. Most of the cephalometric analyses in patients with OSA are based on Sella-Nasion references like the Downs-Northwestern method, whereas the Ricketts format uses three vertical measurements: the facial axis angle, lower facial height, and total facial height (18). According to Ricketts analysis, there are three facial pattern classifications among orthodontic patients: (i) a brachy facial pattern (short face), (ii) a mesio facial pattern (medium face), the average Japanese facial pattern, and (iii) a dolico facial pattern (long face). Analyses of lateral cepholograms of male Japanese OSA patients and non-OSA using Ricketts method indicated that the facial patterns of OSA patients are dolico, where the hyoid bone is positioned low, the soft palate is longer and the width of the airway is narrower than that of the non-OSA controls (7). In contrast, Downs-Northwestern analysis can not detect significant differences between Japanese OSA patients and non-OSA controls (19). The facial pattern with a downward mandible development, characteristic of OSA patients, is confirmed in another comparison study (20). Multivariate regression analysis showed that the BMI and FX were the dominant overall determinants for AHI in 206 Japanese subjects in this study. Other cephalometric variables including the SNA, SNB, and NSBa were not included as independent factors for AHI. These results suggest that the risk factors for OSA may be obesity and a dolico facial pattern seen by Ricketts method. A low FX may contribute to narrowing of the hypopharyngeal space as well as susceptibility to developing OSA. The Ricketts method, and not the Downs-Northwestern method, may thus be suitable for examining craniofacial abnormalities of Japanese patients with OSA.

The characteristics of the craniofacial bony structure in non-obese Japanese patients with OSA were previously analyzed in a smaller sample size (15–17). Observed alterations in variables based on Sella-Nasion references in craniofacial morphology were inconsistent among several reports. We found that severe OSA patients had a smaller SNA and SNB compared with mild and moderate OSA patients in the non-obese group. A smaller SNA and SNB is associated with maxilla and mandibular retrusion relative to the nasion, and is related to the backward displacement of the attached soft tissue (21, 22). The upper-airway size is determined by skeletal factors and soft-tissue. In obese patients, increased adipose tissue in the neck may predispose the airway to narrowing even though craniofacial skeletal abnormalities may be absent. Previous studies using cephalometric analysis for Japanese OSA revealed that upper airway soft tissue...
enlargement plays a more important role than does bony abnormalities in the development of OSA in obese patients (15, 17). We did not find any differences in four cephalometric variables between severe and mild to moderate OSA patients in the obese group, suggesting that the deposition of adipose tissue in the upper airway may aggravate the severity of OSA in this group. Soft tissue cephalometric norms are specific for ethnic groups (23). Statistically significant differences were found in the soft tissue measurements of Japanese lateral cephalometric radiographs when compared with Caucasian norms. Therefore, new specific parameters might have to be introduced to evaluate the soft tissue cephalometric features of Japanese patients with OSA.

Furthermore, to focus more on the differences in facial bone structures, we compared obese, mild to moderate OSA patients, who have less severe sleep disordered breathing despite their obesity because they might have more of a bony structure, and non-obese, severe OSA patients, who might suffer more from a small facial structure. This analysis showed that the FX and SNB may be important variables that cause OSA. Although there exists a positive relationship between these two parameters (data not shown), the SNB is the anteroposterior parameter and the FX is the mainly vertical parameter, partly containing the anteroposterior component, for measuring facial bone structure. Thus, there might exist the possibility that the combination of the FX and SNB is useful for evaluating the bony structure of OSA patients.

A p-value of less than 0.05 was considered to indicate statistically significance in this study. The conservative Bonferroni approach involves using a corrected significance value calculated by multiplication of the observed p-value with the number of statistical tests performed. Bonferroni corrections for the total number of tests are probably too conservative (24) because PSG and cephalometric parameters are not independent of each other, and such closely related indexes as seen in this study are probably not independent either. Although we did not correct p-values in the study, further confirmation in other cohorts is required. There exist several limitations in our study. The study subjects did not include normal control without snoring or daytime sleepiness, and the sample number of simple snorers was not sufficient to make a comparison with patients with OSA. All of the subjects were Japanese, and other Asian subjects were not studied, so that racial differences in cephalometry were not made clear. Further studies involving multiracial subjects are therefore needed.

Conclusions

The risk factors for OSA in Japanese men may be obesity and a dolico facial pattern seen by Ricketts method. A smaller SNA and SNB seem to be associated with the severity of OSA in non-obese patients, and adipose tissue deposits in the upper airway may aggravate the severity of OSA in obese patients. These findings need to be confirmed in other Asian subjects.

References

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