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Obesity and Craniofacial Abnormalities are Independent Causal Factors for Obstructive Sleep Apnea-Hypopnea Syndrome

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SUMMARY

OBJECTIVES : Obstructive sleep apnea-hypopnea syndrome is characterised by recurrent episodes of functional pharyngeal airway obstruction during sleep. Here, we examined the craniofacial characteristics and body mass index of patients with obstructive sleep apnea-hypopnea syndrome and healthy counterparts, and investigated the relationship between these factors and onset of obstructive sleep apnea-hypopnea syndrome.

MATERIAL AND METHODS : Sixty non-edentulous male with obstructive sleep apnea-hypopnea syndrome diagnosed by conventional polysomnography were divided into two groups according to their body mass index, which was used as an index of obesity ($<25\,kg/m^2$: non-obese, $\geq 25\,kg/m^2$: obese). Craniofacial characteristics were analysed by cephalogram using Ricketts' method and the Downs-Northwestern method.

RESULTS : The mean body mass index was greater in patients with obstructive sleep apnea-hypopnea syndrome compared with their healthy counterparts. As for the craniofacial characteristics of patients with obstructive sleep apnea-hypopnea syndrome, the mandible was relatively small and located posteriorly, and the hyoid bone was at a lower position. However, in patients with obstructive sleep apnea-hypopnea syndrome, there was no significant difference in any of the cephalometric measurements between non-obese and obese patients.

CONCLUSION : Obesity and craniofacial skeletal abnormalities are non-reciprocal, independent causal factors for obstructive sleep apnea-hypopnea syndrome.

Key Words : Obstructive sleep apnea-hypopnea syndrome, Cephalogram, Ricketts' analysis, Body mass index

INTRODUCTION

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterised by recurrent episodes of functional pharyngeal airway obstruction during sleep[1]. OSAHS has attracted significant attention because of its deleterious effects on daytime alertness and cardiovascular functions[2]. OSAHS is reported to be caused by local anatomical factors such as craniofacial anomalies[2~5], adenoid or tonsillar hypertrophy, macroglossia, redundant or hypertonic oropharyngeal soft tissue, and mandibular hypoplasia[6]. We previously examined the relationship between onset of OSAHS and craniofacial characteristics, and found that the length of the man-

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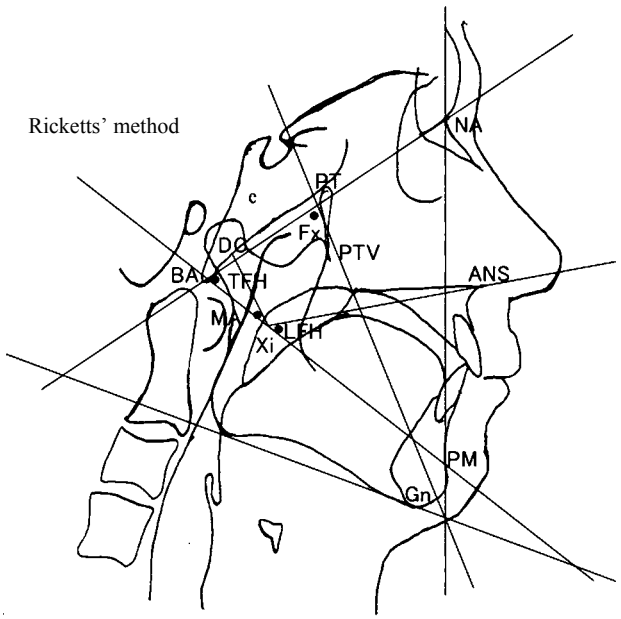

Fig. 1 cephalometric landmarks and lines
NA (nasion) : anterior point at the front nasal suture, BA (basion) : the midpoint of the anterior border of the foramen magnum, PT (pterygoid point) : the lower margin of the foramen rotundum, PM (protuberance menti) : the upper margin of the mental protuberance, Xi : the point of mandibular foramen, DC (condyle centre) : the centre point of the condyle on the BA-NA plane, PTV (pterygoid root vertical) : posterior region of the pterygopalatine fossa, Gn (gnathion) : the most inferior point in the contour of the chin, ANS (anterior nasal spine) : the most anterior part of the nasal floor.

dibular body in patients with OSAHS was shorter than that in healthy counterparts (Narikawa K, Imai Y, Sasaki T, et al : Comparison of Ricketts' analysis and Downs-Northwestern analysis in lateral cephalogram of sleep apnea syndrome. *Proc IADR* : 130. 2002). Moreover, the position of the mandible of patients with OSAHS is located at a posterior site when compared with that of healthy counterparts, and the position of the hyoid bone in the patients is located at a lower position than that of healthy counterparts[7]. It is also known that OSAHS is caused by not only craniofacial characteristics but also by obesity.

In the present study, we examined the craniofacial characteristics and body mass index (BMI) in patients with OSAHS and healthy counterparts, and investigated the relationship between these factors and the onset of OSAHS.

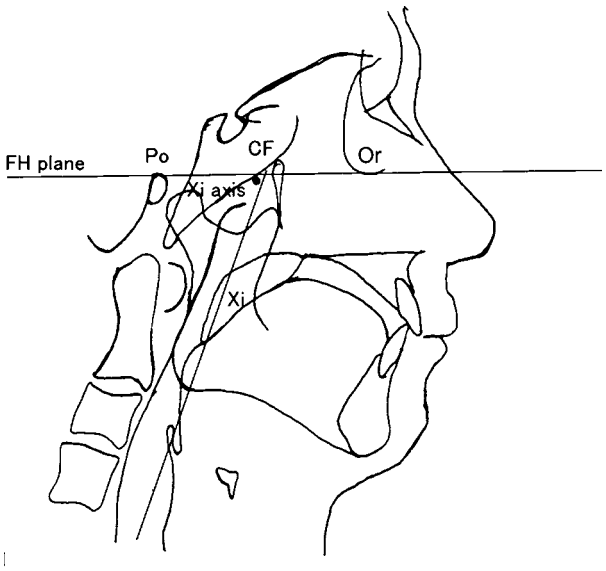

Fig. 2 cephalometric landmarks and lines
Po (porion) : most superior point of the auditory meatus, FH plane (Frankfort plane) : line from Or to Po.

PATIENTS AND METHODS

Patients

Only non-edentulous male were included in the study. A total of 60 cases of OSAHS were diagnosed by polysomnography at the Department of Neurology, Dokkyo University School of Medicine between August 1998 and April 2005. All of the patients were referred to our department for treatment with an oral appliance (OA). And these subjects were patients with OSAHS of mild or moderate, whom the department of neurology requested creation of OA. We created the OA after analysing their cephalometry. The patients were divided into two groups according to their BMI. BMI was used as an index of obesity (BMI $<25\,kg/m^2$: non-obese, BMI $\geq 25\,kg/m^2$: obese), and the craniofacial characteristics were analysed by cephalogram using Ricketts' method and the Downs-Northwestern method (Fig. 1-3). Consent was obtained from each patient for the use of their data in the study.

Cephalometric analysis

Control groups are 40 male volunteers who work in the Dokkyo Medical University hospital. We checked that they are not OSAHS by inquiry or a check sheet. The cephalometric landmarks used in this study were as follows : sella (S), the centre of the hypophyseal

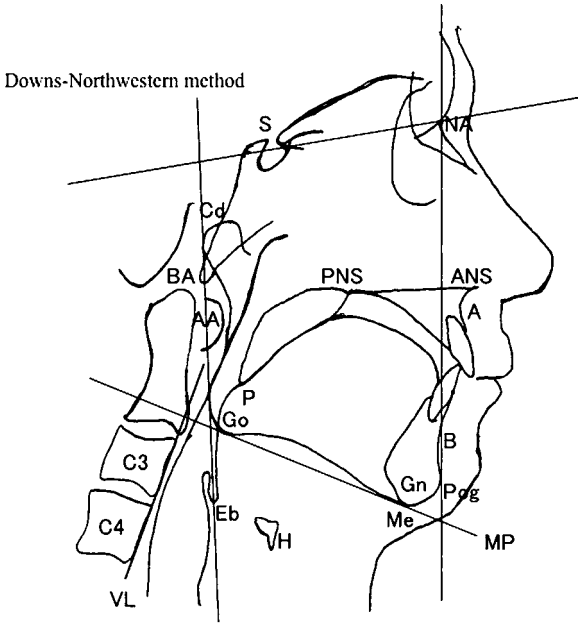

Fig. 3 cephalometric landmarks and lines
S (sella) : the centre of the hypophyseal fossa (sella turcica), A (subspinale) : the deepest point on the premaxillary outer contour between the anterior nasal spine and the central incisor ; B (supramentale) : the deepest point on the outer mandibular contour between the mandibular incisor and the pogonion (Pog), ANS (anterior nasal spine) : the most anterior part of the nasal floor, PNS (posterior nasal spine) : the most posterior part of the contour of the hard palate, Gn (gnathion) : the most inferior point in the contour of the chin, Go (gonion) : the most posterior point on the convexity of the angle of the mandible, Pog (pogonion) : the furthest bulging point of the mentum, Me (menton) : most inferior point of the chin bone, AA (anterior atlas), VL (vertebrae line) : a line across C3 and C4, H (hyoid) : the most anterior-superior point on the body of the hyoid, mandibular condyle (Cd) : the highest point on the mandibular condyle, P (soft palate) : lowest point of the soft palate, MP (mandibular plane) : a plane constructed from Me through Go.

fossa (sella turcica) ; porion (Po), most superior point of the auditory meatus ; nasion (NA), anterior point at the front nasal suture ; orbite (Or), most inferior point of orbital floor ; subspinale (A), the deepest point on the premaxillary outer contour between the anterior nasal spine and the central incisor ; supramentale (B), the deepest point on the outer mandibular contour between the mandibular incisor and the pogonion (Pog) ; anterior nasal spine (ANS), the most anterior part of the nasal floor ; posterior nasal spine (PNS), the most posterior part of the contour of the hard palate ; gnathion (Gn), the most inferior point in the contour of the chin ; gonion (Go), the most posterior point on the convexity of the angle of the mandible ; pogonion (Pog), the furthest bulging point of the mentum ; menton (Me), most inferior point of the chin bone ; anterior atlas (AA) ; vertebrae line (VL), a line across C3 and C4 ; hyoid (H), the most anterior-superior point on the body of the hyoid bone ; soft palate (P) ; lowest point of the soft palate ; basion (BA), the midpoint of the anterior border of the foramen magnum ; pterygoid point (PT), the lower margin of the foramen rotundum ; protuberance menti (PM), the upper margin of the mental protuberance ; the point of mandibular foramen (Xi) ; condyle centre (DC), the centre point of the condyle on the BA-NA plane ; mandibular condyle (Cd), the highest point on the mandibular condyle ; centre of Frankfurt (CF), cross point of the FH plane and pterygoid root vertical ; pterygoid root vertical (PTV), posterior region of the pterygopalatine fossa.

The following angles in degrees and dimensions in millimetres were measured : SNA [angle between lines S-NA and NA-A], SNB [angle between lines S-NA and NA-B], ANB [angle between lines NA-A and NA-B], Gn-Cd [distance from Gn to Cd], Pog-Go [distance from Pog to Go], MP-H [distance from mandibular plane to H], ANS-H [distance from ANS to H], N-BA [distance from N to BA], BA-PNS (bony nasopharynx) [distance from PNS to BA], AA-PNS (bony oropharynx) [distance from AA to PNS], ANS-PNS [distance from ANS to PNS], H-VL [distance along a perpendicular plane from H to VL], Fx (facial axis) [angle between lines PT-Gn and NA-BA], LFH (lower facial height) [angle between lines Xi-ANS and Xi-PM], TFH (total facial height) [angle between lines NA-BA and Xi-PM], Xi axis [angle between lines FH plane and CF-Xi], MA (mandibular arc) [angle between lines DC-Xi and Xi-PM], and Xi-PM [distance from PM to Xi point].

Statistical analysis

Basic statistical analyses were performed by the Mann-Whitney U test using Stat-View 5.0 software (SAS Institute, Inc., Cary, NC, USA). The results were considered significant if the probability was <0.05.

Table 1 Comparison of cephalometric measurements

	OSAHS (n=60)	Control (n=40)	p value
Angular measurements : Degrees			
Fx *	74.7±12.6	82.2±4.4	0.0026
LFH *	59.5±13.1	50.0±4.9	<0.0001
TFH	64.8±5.6	63.0±5.9	0.1991
Xi axis	71.1±4.0	72.2±3.5	0.1555
MA	34.7±8.0	35.9±6.1	0.4204
SNA	81.1±3.6	81.5±3.3	0.5686
ANB	3.8±3.0	3.5±3.1	0.5305
SNB	77.3±4.3	77.9±3.4	0.3715
Linear measurements : mm			
Xi-PM	75.3±5.7	76.5±5.1	0.2251
Gn-Cd *	127.3±7.4	131.6±6.7	0.0034
Pog-Go *	80.5±5.2	83.0±5.2	0.0369
MP-H *	21.2±5.7	16.5±5.8	0.0002
ANS-H *	101.8±7.0	97.7±6.9	0.0052

* significant difference Data are presented as mean±S.D.

Fx (facial axis) : angle between lines PT-Gn and NA-BA, LFH (lower facial height) : angle between lines Xi-ANS and Xi-PM, TFH (total facial height) : angle between lines NA-BA and Xi-PM, Xi axis : angle between lines FH plane and CF-Xi, MA (mandibular arc) : angle between lines DC-Xi and Xi-PM, SNA : angle between lines S-NA and NA-A, ANB : angle between lines A-NA and NA-B, SNB : angle between lines S-NA and NA-B, Xi-PM : distance from PM to Xi point, Gn-Cd : distance from Gn to Cd, Pog-Go : distance from Pog to Go, MP-H : distance from mandibular plane to H, ANS-H : distance from ANS to H.

RESULTS

1. BMI in patients with OSAHS and healthy counterparts

The BMIs of the patients with OSAHS and healthy counterparts were 25.0±3.6 kg/m^2 and 23.2±3.4 kg/m^2, respectively. The age of the patients with OSAHS and healthy counterparts were 38.0±7 and 36.6±10, respectively. The mean BMI was greater for patients with OSAHS compared with that for healthy counterparts (p=0.0003). The number of obese (BMI ≥ 25 kg/m^2) subjects was 39, and the number of non-obese subjects (BMI <25 kg/m^2) was 61. For the obese subjects, the number of patients with OSAHS (32 persons, 84%) was significantly greater than the number of healthy counterparts (7 persons, 16%) (p=0.0015). For the non-obese subjects, there was no significant difference between the number of patients with OSAHS (28 persons, 46%) and healthy counterparts (33 persons, 54%).

Table 2 Mean age and BMI for non-obese and obese patients with OSAHS

	Non-obese (n=28)	Obese (n=32)
Age	37.3±9.4	38.6±5.2
BMI	22.1±3.4	27.6±4.6

Data are presented as mean±S.D.

2. Relationship of the craniofacial characteristics in the patients with OSAHS and healthy counterparts

Details of the cephalometric measurements of patients with OSAHS and the healthy counterparts are given in Table 1. The mean Fx was significantly smaller in patients with OSAHS (74.7±12.6°) than in healthy counterparts (82.2±4.4°) (p=0.0026). The mean LFH was significantly greater in patients with OSAHS (59.5±13.1°) than in healthy counterparts (50.0±4.9°) (p<0.0001). The mean Gn-Cd was significantly smaller in patients with OSAHS (127.3±7.4 mm) than in healthy counterparts (131.6±6.7 mm) (p=0.0034). The mean Pog-Go was significantly smaller in patients with OSAHS (80.5±5.2 mm) than

Table 3 Comparison of cephalometric measurements with OSAHS

	Non-obese (n=28)	Obese (n=32)	p value
Angular measurements : Degrees			
Fx	72.8±12.2	76.4±12.8	0.1847
LFH	61.0±13.1	58.2±13.2	0.4498
TFH	66.2±4.9	63.7±5.9	0.1095
Xi axis	70.3±3.6	72.2±3.7	0.0585
MA	34.6±9.6	34.8±6.3	0.5784
SNA	80.7±4.3	81.4±2.9	0.2271
ANB	4.1±3.2	3.5±2.8	0.4235
SNB	76.8±4.7	77.7±3.9	0.5385

Data are presented as mean±S.D.

Table 4 Comparison of cephalometric measurements with OSAHS

	Non-obese (n=28)	Obese (n=32)	p value
Linear measurements : mm			
Xi-PM	74.5±5.9	76.0±5.6	0.5773
Gn-Cd	126.1±7.5	128.3±7.2	0.2886
Pog-Go	80.2±5.5	80.9±5.0	0.5878
MP-H	21.0±6.8	21.4±4.6	0.6611
ANS-H	101.4±6.7	102.2±7.3	0.49
N-BA	112.6±5.5	112.1±5.1	0.5243
BA-PNS	48.3±5.4	48.4±5.0	0.9619
AA-PNS	36.8±4.1	38.1±4.6	0.1973
ANS-PNS	54.3±3.8	54.1±5.5	0.633
H-VL	39.9±5.9	41.9±5.6	0.3727

Data are presented as mean±S.D.
N-BA : distance from N to BA, BA-PNS (bony nasopharynx) : distance from PNS to BA, AA-PNS (bony oropharynx) : distance from AA to PNS, ANS-PNS : distance from ANS to PNS, H-VL : distance along a perpendicular plane from H to VL.

in healthy counterparts (83.0±5.2 mm) (p=0.0369). The mean MP-H was significantly greater in patients with OSAHS (21.2±5.7 mm) than in healthy counterparts (16.5±5.8 mm) (p=0.0002). The mean ANS-H was significantly greater in patients with OSAHS (101.8±7.0 mm) than in healthy counterparts (97.7±6.9 mm) (p=0.0052). Other factors (TFH, Xi axis, mandibular arc, SNA, ANB, SNB, and Xi-PM) were similar in patients with OSAHS and healthy counterparts (Table 1). As for the craniofacial characteristics of patients with OSAHS, the mandible was relatively small and located posteriorly, and the hyoid bone was located at a lower position.

3. Subdivision of the patients

Sixty patients with OSAHS were examined. The patients were divided into two groups according to BMI (cut-off point=25) ; one group comprised 28 non-obese patients (mean BMI : 22.1±3.4 kg/m^2) and the other group comprised 32 obese patients (mean BMI : 27.6±4.6 kg/m^2). There was no significant difference in age between non-obese and obese patients with OSAHS (Table 2 ; p=0.8879). Details of the cephalometric measurements of the two groups are shown in Tables 3 and 4. There was no significant difference in the cephalometric measurements between the two groups.

DISCUSSION

The clinical symptoms of OSAHS are well established, but the underlying abnormalities associated with development of obstruction of the upper airway during sleep are still subject to debate. Treatments should target the causative abnormalities rather than the symptoms of OSAHS[2]. In this study, we demon-

strated that either obesity or craniofacial abnormalities are causal factors for OSAHS. Interestingly, in patients with OSAHS, there was no significant difference in age and any of the cephalometric measurements between non-obese and obese patients. These results suggest that obesity and craniofacial abnormalities are non-reciprocal, independent causal factors for OSAHS. Non-obese patients with OSAHS do not always have craniofacial abnormalities. However, Paoli et al. (2001) reported that obesity and craniofacial characteristics are reciprocal causal factors for OSAHS[8]. Patients with a high apnea index and a normal weight had craniofacial abnormalities, and patients with a high BMI and a low apnea-hypopnea index showed abnormalities in the soft tissues. In other words, non-obese or slightly obese patients may have a genetic predisposition or craniofacial growth disorder that leads to the development of OSAHS. On the other hand, obese patients have a craniofacial structure with normal cephalometric values, meaning that the dysfunction may be related to the tissue changes induced by obesity. Paoli et al. used a cut-off value of 30 kg/m^2 for BMI as the index for obesity ; however, we used a cut-off value of 25 kg/m^2. It is very rare to encounter a Japanese individual with a BMI over 30 kg/m^2. This may be one of the reasons for the discrepancy between our data and their data. There is also a skeletal difference between Asians and white Caucasian males. Li et al. reported that, in comparing Far-East Asian men with OSAHS to white Caucasian males with OSAHS, Far-East Asian men were found to have a more anteriorly projected maxilla and mandible[9]. We think that many patients with OSAHS are both obese and have craniofacial abnormalities, and we are interested in how these patients compare with those who are only obese or only have craniofacial abnormalities, and whether there is a difference in severity. Yu et al. reported that, compared with non-obese patients with OSAHS, obese patients with OSAHS showed the following craniofacial anatomical characteristics : 1) anteriorly displaced hyoid bone (H-VL) ; 2) longer tongue and soft palate (PNS-P) ; and 3) increased anteroposterior width of the bony nasopharynx (BA-PNS) and oropharynx (AA-PNS)[10]. In our study, a significant difference was not seen, although AA-PNS and H-VL tended to be shorter in non-obese patients with OSAHS compared with obese patients with OSAHS. The difference in the mean age of the study subjects and the mean BMI may be related to the difference in the results. In particular, the mean BMI of obese patients with OSAHS in the study by Yu et al. was 33.5 ± 1.1 kg/m^2, whereas the mean BMI in obese patients with OSAHS in our study was 27.7 ± 4.6 kg/m^2. Furthermore, Yu et al. reported that the inferior and anterior displacement of the hyoid bone in obese patients may therefore be the result of the greater tongue mass and deposition of adipose tissue[10]. In other words, it is thought that the severity of obesity causes a change in the position of the hyoid bone. On the other hand, the anteroposterior width of the bony nasopharynx and oropharynx in non-obese patients with OSAHS is narrower than that in obese patients with OSAHS. Our data show that the lower jaw in patients with OSAHS is located in a lower position compared with healthy counterparts. Therefore, the anteroposterior width of the bony nasopharynx and oropharynx may become narrow with the downward rotation of the lower jaw. This research mainly examined the craniofacial skeletal abnormalities. It is necessary to analyse in detail and to examine the validity of these opinions about the difference in soft tissue. This is a subject for future study.

Jamieson et al. observed that patients with OSAHS have craniomandibular abnormalities and concluded that patients with OSAHS have normally positioned maxillas, rerouted mandibles, large cranial deflections, long soft palates, and low-positioned hyoid bones[2]. The results of the present study are compatible with their results.

We utilised Ricketts' method in addition to the Downs-Northwestern method for the analysis of craniofacial characteristics. Ricketts' method, reported to have an advantage for assessing the vertical structure of the face[11,12], uses three vertical measurements : facial axis, lower facial height, and total facial height. In this study, we first compared SNB, SNA, and ANB that were obtained by the Downs-Northwestern method in patients with OSAHS and healthy counterparts. However, no significant differences were seen in these measurements between the two groups. On the other hand, Fx and LFH, which were obtained by Ricketts' method, were apparently different in the two groups.

Recently, Li et al. reported that mandibular hypoplasia is not a risk factor for the onset of OSAHS[9]. There was no significant difference in the SNB by the Downs-Northwestern method between the patients with OASHS and healthy counterparts in our data as well. However, although there was no significant difference in the SNB, we believe that the mandible is malformed in patients with OSAHS, because the SNB is controlled by the S-N distance. Thus, Ricketts' method may be superior to the Downs-Northwestern method for the analysis of craniofacial characteristics in patients with OSAHS.

A dolico-type craniofacial pattern has been reported in patients with OSAHS. Because the mandible is rotating downwards, Fx and LFH increase, resulting in a dolico pattern. In addition, rotation of the mandible lowers the position of the suprahyoid muscles and hyoid bone.

These abnormalities of craniofacial morphology may also be found in obese patients with OSAHS. Therefore, it is very important to analyse maxillofacial characteristics and provide treatment for these patients.

LIMITATIONS

This study has some limitations. Only Japanese male patients were included. Cephalogram was taken in the sitting position at the time of awakening. And patients with OSAHS are limited to the mild or moderate.

CONCLUSION

Obesity and craniofacial skeletal abnormalities are non-reciprocal, independent causal factors for obstructive sleep apnea-hypopnea syndrome.

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