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Effect of a non-adjustable oral appliance on upper airway morphology in obstructive sleep apnoea

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Summary
Background: To evaluate the effect of oral appliance (OA) on upper airway morphology and its relationship with treatment response in subjects with obstructive sleep apnoea (OSA).
Methods: Symptomatic OSA subjects were recruited. Non-adjustable OA was custom made. Variables examined at baseline and while wearing the device at 2 months included polysomnographic data, computed tomographic measurements of upper airway cross sectional area at level of velopharynx (VA) and hypopharynx (HA), upper airway volume, and cephalometric parameters. Treatment outcome was based on post-treatment apnoea–hypopnoea index (AHI).
Results: Forty patients were recruited and 23 (7 women) completed the study. They were middle-aged (49, 40–58 years) (median, interquartile range) and overweight (BMI 26, 23.3–29.5 kg/m^2), with moderate OSA (AHI 26.4, 14.1–36). The overall post treatment AHI was 8.4 (2.4–12.5), with 14 (61%) patients showing good response (AHI <10), and the other 9 patients showing moderate response ($>50\%$ reduction in AHI but still $\geqslant 10$). OA decreased the cross-sectional area of the HA ($P = 0.046$), showed a trend of decreasing the ratio of cross-sectional area of the HA to cross-sectional area of the VA ($P = 0.053$) and significantly increased the overall upper airway volume ($P = 0.006$, $n = 11$). No significant relationship between upper airway parameters and treatment outcome was identified.
Conclusions: OA altered upper airway morphometry towards a profile consistent with decreased propensity to collapse, which may thus have contributed to improvement of OSA.

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Introduction

Oral appliance (OA) has been suggested as an alternative treatment in patients with mild to moderate obstructive sleep apnoea (OSA), and who cannot tolerate continuous positive airway pressure (CPAP),[1–4] but treatment response varies in individuals. Understanding the working mechanisms of OA and predictors of treatment response will help in selecting appropriate candidates for this treatment. Changes in morphology and dimensions of the upper airway, and increase in upper airway muscular tone, resulting in less collapsible upper airway, have been proposed to be the working mechanisms of OA.[5–9] This study was designed to evaluate the effects of OA on upper airway parameters and their relationship with treatment response.

Materials and methods

Patient recruitment

Consecutive patients who attended Sleep Laboratory at Queen Mary Hospital for suspected OSA were interviewed after diagnostic polysomnogram (PSG). Patients with mild to moderate OSA were recruited for OA treatment with written consent. Other inclusion criteria included: age >18 years, excessive daytime sleepiness as evidenced by Epworth sleepiness score (ESS) 9 or above, adequate dentition and ability to protrude mandible forward. Exclusion criteria included inadequate healthy teeth for retention of OA, active periodontal disease, history or presence of temporo-mandibular joint (TMJ) pain and/or trismus, obvious anatomic/pathological airway obstruction, high risk occupation, e.g. driver, or unstable medical disease. Institutional Ethics Committee approved the study.

Study design

After baseline PSG, subjects who fulfilled the relevant study criteria and consented to the study were referred to the orthodontist (SK) for dental assessment. Those who were considered suitable for the device underwent lateral cephalometry and computed tomography (CT) of the upper airway while the device was being fabricated. Subjects were then advised to use the OA every night during sleep. They were re-assessed after using the device for 2 months. At reassessment, compliance and side effects of treatment and symptoms of sleep apnea were documented; lateral cephalometry and CT were repeated as described below.

Oral appliance (Fig. 1)

The OA was made of dental acrylic that was modified from a functional activator (Harvold type). It held the mandible in a forward direction with some vertical opening. The appliances were custom made for individual patients by one orthodontist. The patient was instructed to open and protrude the mandible as far as possible, then to relax and retract the mandible slowly to a comfortable position. This movement was repeated several times until the patient could reach the most advanced position without causing discomfort, and the OA was moulded at this jaw position. If fatigue or soreness developed on wearing the device, a new OA would be prepared with a less protrusive and more comfortable mandibular position.

Sleep study

All subjects underwent overnight PSG at the Sleep Laboratory at Queen Mary Hospital (Alice 3 Diagnostics System, Respironics, Pennsylvania, US) with documentation of sleep stages by electroencephalogram, electro-oculography, and electromyography; respiratory movement by impedance plethysmography; airflow by nasal pressure sensor with thermistor backup, arterial oxygen saturation by pulse oximetry, snoring by tracheal microphone, and sleep position by position sensor. Data were manually scored according to standard criteria.[10–12] The average number of episodes of apnoea and hypopnoea per hour of sleep (the apnoea–hypopnoea index, AHI) was calculated as the summary measurement of sleep disordered breathing. At reassessment, PSG was performed with patients wearing their OA.

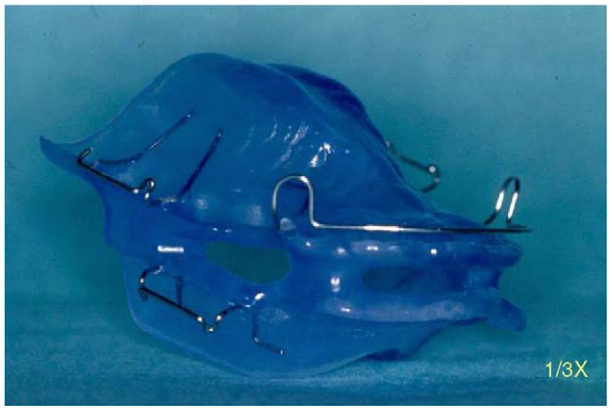


Figure 1 Oral appliance used in this study.

Computed tomography (CT)

All CT examinations were performed with the subject awake and head in a neutral (midway between flexion and extension) supine position using a Hi-speed Advantage scanner (General Electric Medical System, Milwaukee, Wisconsin, USA). Computed tomographic scan of the head and neck region was done for measurement of upper airway cross-sectional areas at two levels: velopharynx (VA) and hypopharynx (HA), upper airway volume as well as cephalometric parameters. The VA and HA cross-sectional area were measured at the tip of the uvula and floor of vallecula, respectively, as determined on the lateral scannogram. Scan parameters included 120 kV, 120 mA, and scan thickness 5 mm with image acquisition obtained during quite tidal breathing. The cross-sectional areas of the upper airway at the VA and HA were manually measured using electronic calipers. The ratio of these two measurements (HA/VA) was also obtained.

Volumetric helical CT scanning of the upper airway was additionally performed in patients who consented. The lateral scannogram allowed selection of scan levels with the hard palate and superior thyroid cornu defining the superior and inferior scan limits. Volumetric data were obtained in full expiration of a quite breath. Scan parameters included 120 Kv, 160 mA, pitch 1:5, scan thickness 5 mm and scan interval 2.5 mm. All data were transferred to a free-standing Graphics workstation, where airway volume was determined using volume rendering three-dimensional CT method to disarticulate air from soft tissues.

Cephalometric measurements were made on the lateral scout view using an electronic cursor at the CT station. Four standard measurements were taken, according to standard protocol[13] for the subsequent purpose of analysis of relationship between the upper airway parameters and adjacent bony anatomy. They were: SNA, the angle between the sellar point, the nasion, and the subspinale; SNB, the angle between the sellar point, the nasion, and the supramentale; ANB, subtract SNB from SNA; and MPH, the shortest perpendicular distance between the plane of the inferior mandibular cortex and the hyoid bone.

Treatment response

This was based on the AHI documented by PSG. A decrease in AHI while wearing OA signified an improvement. Good response was defined as post-treatment AHI <10, moderate response as post-treatment AHI less than 50% of baseline but still $\geqslant 10$, poor responder as post-treatment AHI $\geqslant 50\%$ of baseline AHI.

Statistical analysis

Data are presented as median with interquartile range. Wilcoxon signed rank test was used to compare parameters without and with OA. Mann Whitney test was used for comparison between subjects with different treatment response. Spearman's correlation was used to assess the relationship between various parameters and AHI. Statistical significance was taken at $P<0.05$.

Results

Patient demography and PSG data (Table 1)

Of forty patients referred to the orthodontist, 14 were deemed not suitable for OA due to dental reasons and 26 were recruited into the study with OA fabrication. One patient lost his OA and was unwilling to continue in the study, another two patients refused to come back for re-assessment, giving 23 (7 women) evaluable patients. These patients were middle-aged (49 years, 40–58) and overweight or obese by Asian criteria (body mass index: 26 kg/m^2, 23.3–29.5).[14] They had sympto-

Table 1 Demographic and PSG data.

	Baseline	2 months	*P* value
Body mass index (kg/m^2)	26 (23.3–29.5)	26 (23.8–30.1)	NS
ESS	13 (10–15)	7 (5–11)	0.001
AHI	26.4 (14.1–36)	8.4 (2.4–12.5)	<0.001
Sleep efficiency (%)	79.5 (70.1–90.3)	83.5 (71.2–88.3)	NS
Oxygen saturation $<90\%$ (mins)	16 (8–52)	2.5 (0.5–22.5)	<0.001

All parameters stated by median (interquartile range) unless otherwise stated ESS = Epworth sleepiness score; AHI = apnoea–hypopnoea index.

matic mild to moderate OSA with median AHI and ESS of 26.4 (14.1–36) and 13 (10–15), respectively.

Efficacy, compliance and complications

At reassessment at two months, sleep apnoea improved as a group (Table 1). Fourteen (61%) patients showed good response [AHI decreased from 16.5 (11.9–27.3) to 3.4 (1.9–7.5, $P = 0.001$)] and nine showed moderate response [AHI decreased from 36 (32.5–40.1) to 16.2 (11.4–26.5)]($P = 0.008$). Self-reported compliance was 88% (6 nights per week, 6–8 h per night). Complications of treatment were minor and no subject dropped out of the study due to side effects.

Upper airway parameters

Evaluation while wearing OA at 2 months showed a significant decrease in the cross-sectional area of the HA and a trend of decreasing the HA/VA ratio (Table 2). Fig. 2 demonstrates the cross-sectional change at the HA in a patient as shown on CT.

Only 11 of the 23 patients consented to undergo volumetric CT scans. An increase in upper airway volume after the application of OA was seen in all and the mean upper airway volume changed from 65.7 mm^3 (39.4–77.9) to 70.8 mm^3 (56.3–94.2) ($P = 0.006$).

There was no significant relationship between any of the upper airway parameters and cephalometric variables (data not shown).

Relationship between upper airway parameters and treatment outcome

There was no significant difference between good and moderate responders in cross-sectional areas at VA and HA, HA to VA ratio, and total upper airway volume, either at baseline or while wearing OA. There was no significant correlation between these upper airway variables and AHI, at baseline or wearing OA, nor between their changes with OA (data not shown).

Discussion

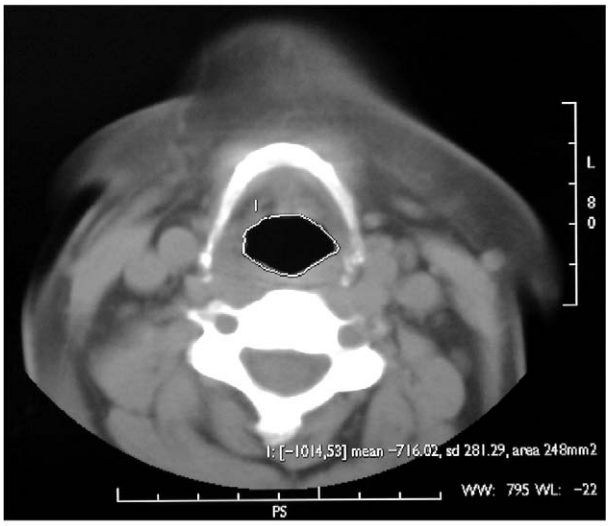
The results of this study showed that OA resulted in improvement of OSA to varying degrees, while the upper airway demonstrated significant decrease in cross-sectional area at the HA, a trend of decrease in HA/VA ratio, and an increase in overall upper airway volume. However, we did not identify any significant relationship between upper airway parameters and treatment outcome.

Previous studies have evaluated upper airway changes with OA using X-ray cephalometry. It has been shown that OA decreased the curvature at the VA while increasing its size, both of which helped to prevent the loss of potential energy which would have led to velopharyngeal collapse.[9] Using magnetic resonance imaging, it has been demonstrated that hypopharyngeal size might decrease or increase depending on the amplitude of mandibular

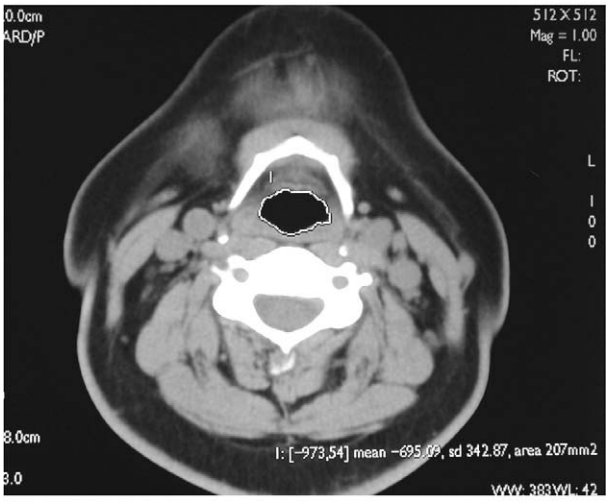
Table 2 Upper airway, cephalometric and dental parameters with and without OA.

	Baseline	2 months (with OA)	*P* value
Upper airway and cephalometric measurements on CT			
Velopharynx airway, VA (mm^2)	157 (110–261)	200 (135–315)	NS
Hypopharyx airway, HA (mm^2)	369 (301–478)	307 (242–451)	0.046
HA/VA	2.21 (1.48–4.11)	1.62 (1.24–2.16)	0.053
Upper airway volume (mm^3)*	65.7 (39.4–77.9)	70.8 (56.3–94.2)	0.006
SNA (°)	96 (90–101)	96 (93–100)	NS
SNB (°)	90 (88–95)	91 (89–97)	NS
ANB (°)	6 (2–7)	5 (2–7)	NS
MPH (mm)	21 (16–24)	15 (8–18)	<0.001
Dental parameters on lateral cephalometric radiograph			
Incisal separation (mm)		8.5 (7.8–10.5)	
Advancement (mm)		5 (3.4–6.3)	

All parameters stated by median (interquartile range) unless otherwise stated.
SNA = angle between the sellar point, the nasion, and the subspinale; SNB = angle between the sellar point, the nasion, and the supramentale; ANB = subtract SNB from SNA; MPH = shortest perpendicular distance between the plane of the inferior mandibular cortex and the hyoid bone.
*Numbers of subjects = 11.



(a)



(b)

Figure 2 CT cross-section at level of hypopharynx without OA (a) and while wearing OA (b).

advancement and vertical opening of incisors.[15] We were not able to find any significant increase in velopharyneal area, but we showed a selective decrease in the hypopharyngeal lumen and the HA to VA ratio. This finding is consistent with previous work, which demonstrated that OA led to significant forward movement of the anterior wall of the VA and the posterior wall of the HA in good responders but not in poor responders.[16] Though the increase in velopharyngeal lumen after OA did not reach statistical significance in our subjects, the overall increase in upper airway volume concomitant with a decrease in the size of the HA would suggest that the size of the VA has increased. Possible explanations for the decrease in hypopharyngeal area are that advancement of the mandible led to a decrease in dilator muscle tone of hypopharyngeal region or a downward shift of the mandible, especially the anterior aspect, which thus encroached on the HA.

The improvement in sleep apnoea despite a decrease in size of part of the upper airway is apparently paradoxical, but previous literature have reported a smaller HA or a relatively larger ratio of the VA to HA in non-OSA subjects compared to OSA subjects.[17–20] Furthermore, uvulopalatopharyngoplasty produced a decrease in the hypopharyngeal area with an increase in velopharyngeal area, and this pattern of change was more pronounced in those who showed good response to the surgery.[20] It has been hypothesized that a smaller HA may protect against the development of OSA, because if the peak inspiratory suction pressure could be damped down at the relatively narrowed HA, the more collapsible VA would be less prone to close.[19] Hence, the morphological changes of the upper airway with OA seen in this study is consistent with a reversal of the predisposing configuration, and may explain the therapeutic effect of the device, while the failure to achieve, in addition, a significant increase in VA size, may explain its limited efficacy compared to other treatment modalities like CPAP.

The overall increase in upper airway volume after OA application suggests that it is one of the mechanisms by which OA improves OSA. Although it is controversial whether OSA subjects have a narrower upper airway,[21,22] it is reasonable that a larger lumen will allow a smaller risk of obstruction when the upper airway is subjected to the same dynamic collapsing force. Studies have reported that OA resulted in less collapsible upper airway in OSA subjects.[8,9]

All subjects in this study showed some improvement in sleep apnoea after OA, albeit to varying extents. We were not able to demonstrate any relationship between changes in upper airway parameters and improvement in sleep apnoea. This is not surprising in view of the complex pathophysiologic mechanisms underlying the development of OSA, which would involve an interplay of anatomic factors and neuromuscular dynamics at the upper airway and not merely physical dimensions of the upper airway, given the limited sample size.

This study has several limitations. Imaging evaluations were performed with the patient awake, which may not reflect the anatomical-physiological conditions during sleep. Logistically, it is extremely difficult to image the upper airway with CT or X-ray during sleep. Another limitation is that non-adjustable OA were used instead of adjustable ones. It is possible that adjustable OA may result in further advancement of the mandible

with better treatment outcome,[23] and thus allow better discrimination of the upper airway changes associated with treatment response. Nonetheless, it has been shown that an advancement of 67% of the maximum value produced the same effect on upper airway morphometry as maximum advancement.[16] Finally, the relatively small sample size with large individual variation in baseline characteristic could have limited the power to identify some of the upper airway changes and the relationships to treatment response.

In summary, our findings suggest that OA can modify upper airway morphology and the resultant profile may favor less dynamic collapse of the upper airway. This may be one of the mechanisms by which OA improves OSA.

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References

1. White J, Cates C, Wright J. Continuous positive airways pressure for obstructive sleep apnea (Cochrane Review). *The Cochrane Library* 2003(Issue 4).
2. Shimidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S. Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. *Sleep* 1995;**18**:511–3.
3. Mohsenin N, Mostofi MT, Mohsenin V. The role of oral appliances in treating obstructive sleep apnea. *J Am Dent Assoc* 2003;**134**:442–9.
4. Ferguson KA. The role of oral appliance in the treatment of obstructive sleep apnea. *Clin Chest Med* 2003;**24**(2):355–64.
5. Ryan CF, Love LL, Peat D, Fleetham JA, Lowe AA. Mandibular advancement oral appliance therapy for obstructive sleep apnoea: effect on awake calibre of the velopharynx. *Thorax* 1999;**54**:972–7.
6. Woodson BT, Feroah T, Connolly LA, Toohill RJ. A method to evaluate upper airway mechanics following intervention in snorers. *Am J Otolaryngol* 1997;**18**:306–14.
7. Yoshida K. Effect of a prosthetic appliance for treatment of sleep apnea syndrome on masticatory and tongue muscle activity. *J Prosthet Dent* 1998;**79**:537–44.
8. Ng AT, Gotsopoulos H, Qian J, Cistulli PA. Effect of oral appliance therapy on upper airway collapsibility in obstructive sleep apnea. *Am J Resp Crit Care Med* 2003;**168**:238–41.
9. Tsuiki S, Lowe AA, Almeida FR, Kawahata N, Fleetham JA. Effects of mandibular advancement on airway curvature and obstructive sleep apnea severity. *Eur Respir J* 2004;**23**:263–8.
10. Rechtschaffen A, Kales AA, editors. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. National Institutes of Health Publication no. 204. Washington, DC: Government Printing Office; 1968.
11. American Sleep Disorders Association. EEG arousals: scoring rules and examples. ASDA report. *Sleep* 1992;**15**:173–84.
12. The Report of an American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. *Sleep* 1999;**22**:667–89.
13. Riley R, Guilleminault C, Herran J, Powell N. Cephalometric analyses and flow-volume loops in obstructive sleep apnea patients. *Sleep* 1983;**6**:303–11.
14. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;**363**:157–63.
15. Gao X, Otsuka R, Ono T, et al. Effect of titrated mandibular advancement and jaw opening on the upper airway in nonapneic men: A magnetic resonance imaging and cephalometric study. *Am J Orthod Dentofac. Orthop* 2004;**125**:191–9.
16. Tsuiki S, Hiyama S, Ono T, et al. Effects of a titratable oral appliance on supine airway size in awake non-apneic individuals. *Sleep* 2001;**24**:554–60.
17. Kuna ST, Bedi DG, Ryckman C. Effect of nasal positive pressure on upper airway size and configuration. *Am Rev Respir Dis* 1988;**138**:969–75.
18. Lam B, Ooi CGC, Peh WCG, et al. Computed tomographic evaluation of the role of craniofacial and upper airway morphology in obstructive sleep apnea in Chinese. *Resp Med* 2004;**98**:301–7.
19. Polo OJ, Tafti M, Fraga J, Porkka KVK, Dejean Y, Billiard M. Why don't all heavy snorers have obstructive sleep apnea? *Am Rev Respir Dis* 1991;**143**:1288–93.
20. Shepard JW, Thawley SE. Evaluation of the upper airway by computerized tomography in patients undergoing uvulopalatopharyngoplasty for obstructive sleep apnea. *Am Rev Respir Dis* 1989;**140**:711–6.
21. Chen NH, Li KK, Li SY, et al. Airway assessment by volumetric computed tomography in snorers and subjects with obstructive sleep apnea in a Far-East Asian population (Chinese). *Laryngoscope* 2002;**112**:721–6.
22. Arens R, McDonough JM, Corbin AM, et al. Upper airway size analysis by magnetic resonance imaging of children with obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2003;**167**:65–70.
23. Tsai WH, Vazquez JC, Oshima T, et al. Remotely controlled mandibular positioner predicts efficacy of oral appliances in sleep apnea. *Am J Respir Crit Care Med* 2004;**170**:366–70.