RESEARCH ARTICLE

Analyses of aerodynamic characteristics of the oropharynx applying CBCT: obstructive sleep apnea patients versus control subjects

^{1,2}Hui Chen, ³Yingguang Li, ³Johan HC Reiber, ⁴Jan de Lange, ⁵Shengxian Tu, ¹Paul van der Stelt, ²Frank Lobbezoo and ²Ghizlane Aarab

¹Department of Oral Radiology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, Netherlands; ²Department of Oral Kinesiology, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, Netherlands; ³Division of Image Processing, Department of Radiology, Leiden University Medical Centre, Leiden, The Netherlands; ⁴Department of Oral and Maxillofacial Surgery, Academic Centre for Dentistry Amsterdam (ACTA) and Academic Medical Centre (AMC), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, Netherlands; ⁵Biomedical Instrument Institute, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China

Objectives: To determine the most relevant aerodynamic characteristic of the oropharynx related to the collapse of the upper airway in obstructive sleep apnea (OSA) patients; and to determine the correlation between the most relevant aerodynamic characteristic(s) of the oropharynx and anatomical characteristics of the oropharynx in OSA patients.

Methods: 31 mild to moderate OSA patients (mean $\pm$ SD age = 43.5 ± 9.7 years) and 13 control subjects (mean $\pm$ SD age = 48.5 ± 16.2 years) were included in this prospective study. The diagnosis of OSA patients was based on an overnight polysomnographic recording. To exclude the presence of OSA in the control subjects, they were asked to fill out a validated questionnaire to determine the risk of OSA. NewTom5G cone beam CT (CBCT) scans were obtained from both OSA patients and control subjects. Computational models of the oropharynx were reconstructed based on CBCT images. The aerodynamic characteristics of the oropharynx were calculated based on these computational models. Pearson correlation analysis was used to analyse the correlation between the most relevant aerodynamic characteristic(s) and anatomical characteristics of the oropharynx in OSA patients.

Results: Compared with controls, the airway resistance during expiration (R_{ex}) of the OSA patients was significantly higher ($p = 0.04$). There was a significant negative correlation between R_{ex} and the minimum cross-sectional area (CSA_{min}) of the oropharynx ($r = -0.41$, $p = 0.02$), and between R_{ex} and the volume of the oropharynx ($r = -0.48$, $p = 0.01$) in OSA patients. After excluding an outlier, there is only significant correlation between R_{ex} and the CSA_{min} of the oropharynx ($r = -0.45$, $p = 0.01$).

Conclusions: Within the limitations of this study, we concluded that the most relevant aerodynamic characteristic of the oropharynx in the collapse of the upper airway in OSA patients is R_{ex} . Therefore, the repetitive collapse of the upper airway in OSA patients may be explained by a high R_{ex} , which is related to the CSA_{min} of the oropharynx.

Dentomaxillofacial Radiology (2018) 47, 20170238. doi: [10.1259/dmfr.20170238](https://doi.org/10.1259/dmfr.20170238)

Cite this article as: Chen H, Li Y, Reiber JHC, de Lange J, Tu S, van der Stelt P, et al. Analyses of aerodynamic characteristics of the oropharynx applying CBCT: obstructive sleep apnea patients versus control subjects. *Dentomaxillofac Radiol* 2018; 47: 20170238.

Keywords: obstructive sleep apnea; cone beam computed tomography; airway resistance; computational fluid dynamics.

Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder, characterized by recurrent obstructions of the airflow in the upper airway,^{1,2} often associated with compromised upper airway space and an increase in upper airway collapsibility.³ The most common complaints of OSA patients are excessive daytime sleepiness, unrefreshing sleep, poor concentration and fatigue.⁴ The real pathogenesis of OSA is still unknown.⁵ However, both anatomical and functional abnormalities of the upper airway may play an important role in the repetitive collapse of the upper airway.⁶

Various imaging techniques have been used for upper airway analysis, such as multidetector row CT⁷ and MRI.⁸ In recent decades, the use of cone beam CT (CBCT) in dentistry has increased considerably. Due to its high spatial resolution, adequate contrast between the soft tissue and empty space and the relatively low radiation dose compared to multidetector row CT, CBCT can be used to analyse the upper airway anatomy three-dimensionally.⁹

Computational fluid dynamics (CFD) is an engineering tool used to analyse problems involving fluid or air flow, by simulating the way that the fluid or air flow is going through a specific tube or conduit.¹⁰ For this reason, CFD has been introduced to simulate the air flow in the upper airway of OSA patients based on three-dimensional (3D) datasets from CBCT.^{11–13} CFD can provide a qualitative insight into how the air flow is travelling through the upper airway in an intuitive way, by showing the contours of the airflow characteristics, such as air velocity, pressure and wall shear stress.^{12,14,15} CFD also allows quantitative assessment of the air velocity, wall shear stress, wall static pressure and airway resistance.^{16–19} Comparison of the aerodynamic characteristics of the airflow within the oropharynx using CBCT, between OSA patients and control subjects, can add insight into the recurrent obstructions of the airflow in the oropharynx of OSA patients from the perspective of aerodynamics. So far, only one study compared the aerodynamic characteristics of the oropharynx in OSA patients and control subjects, however with a relatively small sample size ($n = 8$).¹³ Based on that study, it is unclear which aerodynamic characteristic of the oropharynx is the most relevant one in the collapse of the upper airway. In this study, we will compare the aerodynamic characteristics of the oropharynx in OSA patients and controls within a relatively large sample size based on CBCT images.

The primary aim of this study was to determine the most relevant aerodynamic characteristic of the oropharynx related to the collapse of the upper airway in OSA patients. The secondary aim was to assess the correlation between the most relevant aerodynamic characteristic(s) of the oropharynx and the anatomical characteristics of the oropharynx in OSA patients.

Methods and materials

Recruitment process

OSA patients were recruited from a prospective study designed to compare two different mandibular advancement device (MAD) therapies in mild and moderate OSA patients (ClinicalTrials.gov.identifier: NCT02724865). The inclusion criteria were: (1) 18 years and older; (2) ability to speak, read and write Dutch; (3) ability to follow-up; (4) ability to use a computer with Internet connection for online questionnaires; (5) diagnosis with symptomatic mild or moderate OSA [$5 \leq$ apnea-hypopnea index (AHI) <30] and (6) Expected to maintain current lifestyle (sports, medicine, diet, etc.).

The exclusion criteria were: (1) untreated periodontal problems, dental pain and a lack of retention possibilities for a MAD; (2) Medication used/related to sleeping disorders; (3) evidence of respiratory/sleep disorders other than OSA (*e.g.* central sleep apnea syndrome); (4) systemic disorders (based on medical history and examination, *e.g.* rheumatoid arthritis); (5) temporomandibular disorders (based on the function examination of the masticatory system); (6) medical history of known causes of tiredness by day, or severe sleep disruption (Insomnia, PLMS, Narcolepsy); (7) known medical history of mental retardation, memory disorders, or psychiatric disorders; (8) reversible morphological upper airway abnormalities (*e.g.* enlarged tonsils); (9) inability to provide informed consent; (10) simultaneous use of other modalities to treat OSA and (11) previous treatment with a MAD.

17 control subjects were prospectively recruited from among those who were referred for various diagnostic reasons to the department of Oral and Maxillofacial Radiology of Academic Centre for Dentistry Amsterdam, Netherlands. The inclusion criteria were age >18 years and CBCT images covering the entire upper airway from the level of the hard palate to the base of the epiglottis. The exclusion criteria were edentulousness, presence of a palatal cleft, presence of a craniofacial syndrome and upper airway surgery in the past.

This study was approved by the Medical Ethics Committee of Academic Medical Centre Amsterdam, protocol number: NL44085.018.13. Written informed consent was obtained from all participants.

Polysomnography (PSG)

For the diagnosis of OSA, all 31 patients included in this study underwent an overnight PSG recording (SOMNOscreenTM Plus PSG, Randersacker, Germany) at Onze Lieve Vrouwe Gasthuis West in Amsterdam. PSG included the following variables: electroencephalogram, electro-oculogram, leg and chin electromyograms, electrocardiogram, pulse oximetry, body position, neck microphone, nasal cannula pressure transducer and inductive plethysmography by means of thoracic and abdominal bands. The PSG recordings were scored

Table 1 Baseline demographic characteristics of OSA patients and control subjects

	OSA (31) Mean $\pm$ SD	Control (13) Mean $\pm$ SD	<i>T</i> / <i>X</i> ²	<i>p</i>
Age (years)	43.5 $\pm$ 9.7	48.5 $\pm$ 16.2	-1.28(<i>T</i>)	0.21
Gender	32% (F)	69% (F)	5.1(<i>X</i> ²)	0.02 ^a
BMI (kg m ⁻²)	26.4 $\pm$ 3.0	24.7 $\pm$ 2.1	1.93(<i>T</i>)	0.06 ^b
AHI (time/hour)	15.0 $\pm$ 6.8	N.A.		
Risk (%)	N.A.	11.7 $\pm$ 8.6		

AHI, apnea-hypopnea index; BMI, body mass index; N.A., not applicable; OSA, obstructive sleep apnea.

Risk (%): risk (%) of having OSA, obtained by completing Philips questionnaire.

^a*p* < 0.05.

^bTendency to significance.

manually in a standard fashion.²⁰ Apnea was defined as cessation of airflow $\geq 90\%$ for at least 10 s. Hypopnea was defined as a decrease in airflow of more than 30% for at least 10 s, and an oxygen desaturation greater than 4%.²⁰ The mean AHI of the OSA group, defined as the number of apneas and hypopneas per hour of sleep, is shown in Table 1.

Questionnaire

To evaluate their risk (%) of having OSA, each control subject was asked to complete a validated questionnaire on sleep apnea.¹⁶ This questionnaire was specifically developed to calculate the risk (%) of having OSA. It consists of three sections with a total of 23 questions on personal characteristics, sleep behaviour and health condition. On the basis of their answers to the questionnaire, only 13 controls with a low risk (%) of having OSA were included in this study.

Cone beam CT (CBCT)

The CBCT data sets of the OSA patients and control subjects were obtained using a NewTom 5G CBCT system (QR systems, Verona, Italy), according to the standard imaging protocol of the department of Oral and Maxillofacial Radiology of Academic Centre for Dentistry Amsterdam, Netherlands. During the imaging procedure, automatic exposure control was applied, and the patients were positioned in a supine position with the Frankfort horizontal (FH) plane perpendicular to the floor.¹⁷ They were instructed to maintain light contact between the molars in natural occlusion, to keep quiet breathing and to avoid swallowing and other movements during the scanning period. The exposure settings were 110 kV, 4 mA, 0.3 mm voxel size, 3.6 s exposure time (pulsed radiation) and 18–36 s scanning time, depending on the size of the patient.¹⁷ The CBCT scans were imported into NNT software to obtain a standard head orientation. The re-orientation was performed by using the palatal plane as a reference (anterior nasal spine -posterior nasal spine) parallel to the global horizontal plane in the sagittal view and perpendicular to the global horizontal plane in the axial view.¹⁸ For further analysis, the images were saved as digital imaging and

communications in medicine files. All images were presented to the observers in a room with dimmed light.

Anatomical modelling of the upper airway

Using Amira® (v. 4.1, Visage Imaging Inc., Carlsbad, CA), the automatic process of the oropharynx segmentation was performed following the same protocol as in a previous study.¹⁷ First, a voxel set was built to include all of the information of the oropharynx; second, a new mask was built with its thresholds ranging from -1000 to -400; and third, the superior boundary (*i.e.* the plane across the posterior nasal spine parallel to the FH plane) and the inferior boundary (*i.e.* the plane across the base of the epiglottis parallel to the FH plane) of the oropharynx were selected in the corresponding axial planes and put into the voxel set. Finally, all of the slices between the upper and lower boundaries were selected and put into the voxel set. The minimum cross-sectional area (CSA_{min}), the anteroposterior dimension of CSA_{min} , the lateral dimension of CSA_{min} , the volume of the oropharynx and the length of the oropharynx were calculated by an orthodontist (HC) and confirmed by an oral radiologist (PvdS) based on the segmented oropharynx (Figure 1).¹⁷ By surface triangulation, all the segmented oropharynx models were subsequently converted into 3D standard tessellation language models.

Aerodynamic modelling of the oropharynx

The segmented standard tessellation language models of the oropharynx were exported into ANSYS ICEM CFD 17.0 (ANSYS, Inc., Canonsburg, Pennsylvania) to generate tetrahedral volume meshes. Depending on the complexity of the oropharynx model, a typical grid consisted of about 1,000,000 tetrahedral cells. ANSYS Fluent (ANSYS, Inc.) was used to conduct flow simulation within the oropharynx. The steady-state Reynolds Averaged Navier-Stokes formulation with the $k-\omega$ shear stress transport turbulence model was used to model aerodynamic characteristics within the oropharynx.¹⁹ The air within the oropharynx was considered adiabatic.²¹ Least squares cell-based gradient was used for spatial discretization.^{22,23} Second-order discretization schemes were used for the pressure and momentum equations. The coupling

Figure 1 (a) The segmented oropharynx. V, volume of the oropharynx; L, length of the oropharynx. (b) The minimum cross-sectional area (CSAmin) on the axial slice of the CBCT image. AP, anteroposterior dimension of CSAmin; lateral, lateral dimension of CSAmin. CBCT, cone beam CT; CSA, cross-sectional area.

between the velocity and pressure fields was realized using the SIMPLE algorithm.^{13,21,24} The density of the air within the oropharynx is set as 1.225 kg m^{-3} and the viscosity of the air is set as $1.79\text{E-}05 \text{ kg/m.s}$. One boundary was set at the hard palate plane, and another boundary was set at the base of the epiglottis. The boundary condition consisted of axial velocity at the inlet plane, and no-slip boundary conditions for the oropharynx wall. An inlet volume flow rate of 166 ml s^{-1} (10 l min^{-1}) was used in the flow simulation.^{15,25}

The aerodynamic characteristics, viz., velocity, wall shear stress and wall static pressure, were calculated by an orthodontist (HC) and confirmed by a medical engineer (YL) in each oropharynx model of OSA patients and controls during both inspiration and expiration. The inspiration phase was simulated by setting the inlet plane at the hard palate level and the outlet plane at the base of epiglottis. Vice versa, the expiration phase was simulated by setting the inlet plane at the base of epiglottis, and the outlet plane at the hard palate level.

Based on CFD calculations, the airway resistance (R) was determined using the following formulation:

$$R = \Delta P/Q$$

where, ΔP is the total pressure drop between the inlet and outlet boundaries of the oropharynx, and Q is the volume flow rate within the oropharynx.

Statistical analysis

Whether the data are normally distributed was tested by the Shapiro-Wilk W Test. The Mann-Whitney- U test (for non-normally distributed variables) or Chi-squared test (for categorical variables) and the independent *t*-test (for normally distributed variables) were used to compare the differences in the demographic characteristics between the OSA patients and their controls. Patient characteristics that were significantly different between the two groups were used as covariate(s) in the following between-group analysis. One-way multivariate analysis of covariance was used to compare the differences in aerodynamic and anatomical characteristics between the OSA patients and their controls. In the OSA group, Pearson correlation analysis was used to analyse whether

significant aerodynamic characteristic(s) are correlated with the anatomical characteristics of the oropharynx. A significance level was set at $p < 0.05$.

Results

Contours of the velocity (m s^{-1}), wall shear stress (Pa) and wall static pressure (Pa) for an OSA patient and a control subject during inspiration are shown in Figure 2. Contours of the velocity (m s^{-1}), wall shear stress (Pa) and wall static pressure (Pa) for an OSA patient and a control subject during expiration are shown in Figure 3.

The demographic characteristics of the OSA patients and the control subjects are shown in Table 1. 31 OSA patients and 17 control subjects were recruited in the study, but four control subjects were excluded due to their high risk of having OSA. There was no significant difference in age between OSA patients and control subjects ($p = 0.21$). The OSA patients tended to have a higher body mass index (BMI) than their controls ($p = 0.06$). There was a significant difference in the gender distribution between OSA patients and control subjects ($X^2 = 5.1$, $p = 0.02$): there were fewer females in the OSA group (32%) than in the control group (69%). Therefore, BMI and gender were entered as covariates in the below-described analyses of covariance.

The aerodynamic characteristics within the oropharynx of OSA patients and control subjects are shown in Table 2. There was a significant difference in the airway resistance during expiration (R_{ex}) between OSA patients and control subjects ($F = 2.90$, $p = 0.04$). Compared with control subjects, the R_{ex} of OSA patients was significantly higher. The other aerodynamic characteristics in OSA patients were not significantly different from those in control subjects ($p = 0.08\text{--}0.77$).

The anatomical measurements of the oropharynx of OSA patients and control subjects are shown in Table 3. There were significant differences in the minimum cross-sectional area (CSA_{min}) and the length of the oropharynx between OSA patients and control subjects. The CSA_{min} of the oropharynx of OSA patients, 65.5 (SD 30.7) mm^2 , was significantly smaller than that

Figure 2 Contours of the velocity (m s⁻¹), wall shear stress (Pa) and wall static pressure (Pa) of a typical obstructive sleep apnea patient (a) and control subject (b) during inspiration.

of control subjects, 97.2 (SD 56.5) mm² ($F = 4.26$, $p = 0.01$). The length of the oropharynx of OSA patients, 65.2 (SD 8.1) mm, was significantly longer than that of control subjects, 56.1 (SD 8.1) mm ($F = 19.19$, $p = 0.00$).

The correlation between R_{ex} and anatomical characteristics of the oropharynx in OSA patients is shown in Table 4. There were significant negative correlations between R_{ex} and the CSA_{min} of the oropharynx ($r = -0.41$, $p = 0.02$) and between R_{ex} and the volume of

Figure 3 Contours of the velocity (m s⁻¹), wall shear stress (Pa) and wall static pressure (Pa) of a typical obstructive sleep apnea patient (a) and control subject (b) during expiration.

Table 2 Results of computational fluid dynamics analysis of OSA patients and control subjects during respiration, with gender and body mass index as covariates

Subject	OSA mean $\pm$ SD/median (interquartile range)	Control mean $\pm$ SD/median (interquartile range)	F	p
Maximum velocity during inspiration (m s^{-1})	7.1 ± 5.3	5.1 ± 1.4	1.24	0.31
Maximum wall shear stress during inspiration (Pa)	2.4 ± 2.3	2.4 ± 1.4	0.37	0.77
Minimum wall static pressure during inspiration (Pa)	$-5.0 (-17.2, -3.4)$	$-5.7 (-7.4, -1.9)$	1.21	0.31
Airway resistance during inspiration (R_{in}) (Pa/L/min)	1.2 (0.9, 2.5)	0.96 (0.69, 1.1)	1.95	0.13
Maximum velocity during expiration (m s^{-1})	7.7 ± 5.9	4.9 ± 2.7	2.27	0.09
Maximum wall shear stress during expiration (Pa)	1.26 (0.7, 3.3)	0.83 (0.6, 1.71)	2.25	0.09
Minimum wall static pressure during expiration (Pa)	-21.2 ± 34.3	-8.0 ± 11.3	2.37	0.08
Airway resistance during expiration (R_{ex}) (Pa/L/min)	1.5 (0.7, 2.8)	0.73 (0.42, 1)	2.90	0.04 ^a

OSA, obstructive sleep apnea.

^a $p < 0.05$.

the oropharynx ($r = -0.48$, $p = 0.01$) (Figure 4a,b). After removing an outlier, there was still significant negative correlation between R_{ex} and the CSA_{min} of the upper airway ($r = -0.45$, $p = 0.01$) (Figure 4c).

Discussion

The aerodynamic characteristics within the oropharynx of OSA patients and control subjects were compared based on their CBCT images. The most relevant aerodynamic characteristic of the oropharynx was the airway resistance during expiration (R_{ex}). Subsequently, the R_{ex} was correlated with anatomical characteristics of the oropharynx in OSA patients. The R_{ex} was related to the CSA_{min} of the oropharynx.

Limitations

One limitation is that we have no PSG recordings of the control subjects, because there was no medical need for these recordings. All control subjects, however, have completed a validated questionnaire to certify their low risk of having OSA.¹⁶ Besides, severe OSA patients ($\text{AHI} > 30$) were not included in this study. It is hypothesized that the R_{ex} of severe OSA patients will be much higher than the R_{ex} of controls due to their smaller CSA_{min} .²⁶ This hypothesis needs to be investigated in a future study. Except the oropharynx, the upper airway also includes the nasopharynx and hypopharynx. Another limitation of this study is that only the airway resistance

(R) in the oropharynx was investigated. Obstruction of the nasal cavity could also play a role in the pathogenesis of OSA.^{27,28} Therefore, it could be interesting to set up a model of the entire upper airway to fully understand the pathogenesis of the OSA from the perspective of aerodynamics. However, CFD analysis of the entire upper airway could be time-consuming due to the complex anatomical structure of the nasal cavity, which needs further investigation.

Confounders

There are many risk factors of OSA, such as higher age, elevated BMI and male gender.²⁹ The prevalence of OSA increases with age, with a peak between the ages of 55 and 64 years.³⁰ It is suggested that BMI is the most important risk factor for OSA.³¹ In this study, there was no significant difference in age between OSA patients and control subjects. In addition, BMI of OSA patients tended to be higher than that of control subjects. In this study, 32% of the OSA patients were female, which is in accordance with the prevalence of OSA in the population.³² In the control group, however, 69% of the patients were female. For that reason, in this study, the possible confounding effects of BMI and gender were taken into consideration in the statistical analyses.

Aerodynamic characteristics of the oropharynx

In this study, we simulated the aerodynamic characteristics of OSA patients and control subjects. We found that

Table 3 The mean ($\pm$ SD) of the oropharynx morphology of OSA patients and control subjects, with gender and body mass index as covariates

Variable	OSA	Control	F	p
Minimum cross-sectional area (CSA_{min}) (mm^2)	65.5 ± 30.7	97.2 ± 56.5	4.26	0.01 ^a
Anteroposterior dimension of the CSA_{min} (mm)	5.1 ± 2.2	6.6 ± 2.1	1.39	0.26
Lateral dimension of the CSA_{min} (mm)	13.4 ± 4.4	15.3 ± 4.7	4.13	0.01 ^a
Volume of the oropharynx (cm^3)	11.2 ± 3.7	10.8 ± 4.1	2.10	0.12
Length of the oropharynx (mm)	65.2 ± 8.1	56.1 ± 8.1	19.2	$<0.001^a$

^a $p < 0.05$. OSA, obstructive sleep apnea. CSA, cross-sectional area.

Table 4 Correlation between airway resistance during expiration (R_{ex}) and oropharynx characteristics in OSA patients

	<i>r</i>	<i>p</i>
Minimum cross-sectional area (CSA _{min}) (mm ²)	-0.41	0.02 ^a
Anteroposterior dimension of the CSA _{min} (mm)	-0.25	0.18
Lateral dimension of the CSA _{min} (mm)	-0.24	0.19
Volume of the oropharynx (cm ³)	-0.48	0.01 ^a
Length of the oropharynx (mm)	-0.23	0.21

CSA, cross-sectional area; OSA, obstructive sleep apnea.

^a*p* < 0.05.

the airway resistance of OSA patients is higher than that of control subjects during expiration, which suggests that R_{ex} may be the most relevant aerodynamic characteristic of the oropharynx in the repetitive collapse of the upper airway in OSA patients. A previous study by Powell et al also found that the airway resistance of the OSA patients is higher than that of control subjects.¹³ However, only four controls and four OSA patients were included in their study, and they did not perform between-group statistical analysis, because this was not the aim of their study.¹³ Further, there is no consensus in literature if the collapse of the upper airway is more likely to occur during inspiration^{33,34} or at the end of the expiration.^{35–38} Based on the present study, we concluded that the collapse of the upper airway in OSA patients probably occurs during expiration.

Correlation between aerodynamic characteristics and anatomical characteristics of the oropharynx in OSA patients

In the current study, we found that OSA patients have a smaller CSA_{min} than control subjects, which is consistent with the conclusion of a systematic review wherein the most relevant anatomical characteristic of the upper airway related to the pathogenesis of OSA was a small CSA_{min}.²⁶ Further, we found a negative correlation between the CSA_{min} of the oropharynx and the R_{ex} of the oropharynx (Figure 4c). To the best of our knowledge, no studies have been performed on the correlation between the anatomical characteristics and aerodynamic characteristics of the oropharynx in the OSA patients. However, one study reported that the change in the anatomical characteristics of the upper airway after treatment is related to the change in the airway resistance in OSA patients.¹³ Powell et al found that the airway resistance was significantly decreased after upper airway surgery, which was in agreement with an increase of the oropharynx volume by 120 ± 70%.¹³ Therefore, it is hypothesized that in OSA patients, the smaller CSA_{min} and volume of the oropharynx will result in a higher R_{ex} of the oropharynx and therefore to a higher risk of collapse during sleep.

Clinical relevance

Previous studies have concluded that various OSA therapies (viz., MAD, and upper airway surgery) change the

Figure 4 (a) Correlation between airway resistance during expiration (R_{ex}) and minimum cross-sectional area (CSA_{min}) of the oropharynx; (b) correlation between Rex and volume of the oropharynx; and (c) correlation between Rex and CSA_{min} after removing an outlier.

airflow characteristics within the upper airway of the OSA patients.^{10–12, 35–43} In responders, the airway resistance reduced significantly as a result of treatment, which shows that the repetitive collapse of the upper airway may indeed be explained by the high R of the oropharynx.^{11–14, 44, 45} However, there is still a lack of knowledge on the comparison of the aerodynamic characteristics of the oropharynx between responders and non-responders at baseline, which can help to recognize the non-responders before starting a treatment. These kinds of studies may improve our selection of OSA patients for a certain OSA treatment. Due to the advantages of non-invasiveness, low costs and the often limited amount of time to perform the examination, CFD analysis has gained widespread attention in airway research recently.⁴⁶ Based on CBCT imaging, CFD analysis permits the spatial visualization of the 3D airflow in the oropharynx during both inspiration

and expiration.^{13,46} The specific aerodynamic characteristics of the airflow, such as a higher R_{ex} , could be used to recognize OSA patient and as an estimator for selecting the most appropriate treatment modality for patients with OSA problems.^{13,14,39} However, there is still not enough evidence to support CFD analysis as a clinical routine to predict the treatment outcome before starting these therapies, which needs further investigation.

References

- Aittokallio T, Virkki A, Polo O. Understanding sleep-disordered breathing through mathematical modelling. *Sleep Med Rev* 2009; **13**: 333–43. doi: <https://doi.org/10.1016/j.smrv.2008.09.008>
- De Backer JW, Vos WG, Verhulst SL, De Backer W. Novel imaging techniques using computer methods for the evaluation of the upper airway in patients with sleep-disordered breathing: a comprehensive review. *Sleep Med Rev* 2008; **12**: 437–47. doi: <https://doi.org/10.1016/j.smrv.2008.07.009>
- Ryan CM, Bradley TD. Pathogenesis of obstructive sleep apnea. *J Appl Physiol* 2005; **99**: 2440–50. doi: <https://doi.org/10.1152/japplphysiol.00772.2005>
- Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: a randomized, placebo-controlled trial. *Respiration* 2011; **81**: 411–9. doi: <https://doi.org/10.1159/000319595>
- Pham LV, Schwartz AR. The pathogenesis of obstructive sleep apnea. *J Thorac Dis* 2015; **7**: 1358–72. doi: <https://doi.org/10.3978/j.issn.2072-1439.2015.07.28>
- Lee RWW SK, Cistulli PA. Craniofacial morphology in obstructive sleep apnea: A review. *Clin Pulm Med* 2010; **17**: 189–95.
- Maurer JT, Stuck BA. Update on upper airway evaluation in obstructive sleep apnea. *HNO* 2008; **56**: 1089–97. doi: <https://doi.org/10.1007/s00106-008-1758-2>
- Stuck BA, Maurer JT. Airway evaluation in obstructive sleep apnea. *Sleep Med Rev* 2008; **12**: 411–36. doi: <https://doi.org/10.1016/j.smrv.2007.08.009>
- Guijarro-Martínez R, Swennen GR. Cone-beam computerized tomography imaging and analysis of the upper airway: a systematic review of the literature. *Int J Oral Maxillofac Surg* 2011; **40**: 1227–37. doi: <https://doi.org/10.1016/j.ijom.2011.06.017>
- Luo H, Sin S, McDonough JM, Isasi CR, Arens R, Wootton DM. Computational fluid dynamics endpoints for assessment of adenotonsillectomy outcome in obese children with obstructive sleep apnea syndrome. *J Biomech* 2014; **47**: 2498–503. doi: <https://doi.org/10.1016/j.jbiomech.2014.03.023>
- Huynh J, Kim KB, McQuilling M. Pharyngeal airflow analysis in obstructive sleep apnea patients pre- and post-maxillomandibular advancement surgery. *J Fluids Eng* 2009; **131**: 091101. doi: <https://doi.org/10.1115/1.3192137>
- Mihaescu M, Mylavarapu G, Gutmark EJ, Powell NB. Large eddy simulation of the pharyngeal airflow associated with obstructive sleep apnea syndrome at pre and post-surgical treatment. *J Biomech* 2011; **44**: 2221–8. doi: <https://doi.org/10.1016/j.jbiomech.2011.06.006>
- Powell NB, Mihaescu M, Mylavarapu G, Weaver EM, Guillemainault C, Gutmark E. Patterns in pharyngeal airflow associated with sleep-disordered breathing. *Sleep Med* 2011; **12**: 966–74. doi: <https://doi.org/10.1016/j.sleep.2011.08.004>
- De Backer JW, Vanderveken OM, Vos WG, Devolder A, Verhulst SL, Verbraecken JA, et al. Functional imaging using computational fluid dynamics to predict treatment success of mandibular advancement devices in sleep-disordered breathing. *J Biomech* 2007; **40**: 3708–14. doi: <https://doi.org/10.1016/j.jbiomech.2007.06.022>
- Zhao M, Barber T, Cistulli P, Sutherland K, Rosengarten G. Computational fluid dynamics for the assessment of upper airway response to oral appliance treatment in obstructive sleep apnea. *J Biomech* 2013; **46**: 142–50. doi: <https://doi.org/10.1016/j.jbiomech.2012.10.033>
- Eijsvogel MM, Wiegersma S, Randerath W, Verbraecken J, Wegter-Hilbers E, van der Palen J. Obstructive sleep apnea syndrome in company workers: development of a two-step screening strategy with a new questionnaire. *J Clin Sleep Med* 2016; **12**: 555–64. doi: <https://doi.org/10.5664/jcs.5690>
- Chen H, Aarab G, Parsa A, de Lange J, van der Stelt PF, Lobbezoo F. Reliability of three-dimensional measurements of the upper airway on cone beam computed tomography images. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2016; **122**: 104–10. doi: <https://doi.org/10.1016/j.oooo.2016.04.005>
- Weissheimer A, Menezes LM, Sameshima GT, Enciso R, Pham J, Grauer D. Imaging software accuracy for 3-dimensional analysis of the upper airway. *Am J Orthod Dentofacial Orthop* 2012; **142**: 801–13. doi: <https://doi.org/10.1016/j.ajodo.2012.07.015>
- Younis BA, Berger SA. A turbulence model for pulsatile arterial flows. *J Biomech Eng* 2004; **126**: 578–84. doi: <https://doi.org/10.1115/1.1798032>
- Berry RB, Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology, and Technical Specifications, Version 2.3*. Darien, IL: American Academy of Sleep Medicine; 2016.
- Van Holsbeke C, De Backer J, Vos W, Verdonck P, Van Ransbeeck P, Claessens T, et al. Anatomical and functional changes in the upper airways of sleep apnea patients due to mandibular repositioning: a large scale study. *J Biomech* 2011; **44**: 442–9. doi: <https://doi.org/10.1016/j.jbiomech.2010.09.026>
- Tu S, Barbato E, Köszegi Z, Yang J, Sun Z, Holm NR, et al. Fractional flow reserve calculation from 3-dimensional quantitative coronary angiography and TIMI frame count: a fast computer model to quantify the functional significance of moderately obstructed coronary arteries. *JACC Cardiovasc Interv* 2014; **7**: 768–77. doi: <https://doi.org/10.1016/j.jcin.2014.03.004>
- Li Y, Gutiérrez-Chico JL, Holm NR, Yang W, Hebsgaard L, Christiansen EH, et al. Impact of side branch modeling on computation of endothelial shear stress in coronary artery disease: coronary tree reconstruction by fusion of 3D angiography and OCT. *J Am Coll Cardiol* 2015; **66**: 125–35. doi: <https://doi.org/10.1016/j.jacc.2015.05.008>
- Menter FR. Review of the shear-stress transport turbulence model experience from an industrial perspective. *Int J Comput Fluid Dyn* 2009; **23**: 305–16. doi: <https://doi.org/10.1080/10618560902773387>
- Mylavarapu G, Murugappan S, Mihaescu M, Kalra M, Khosla S, Gutmark E. Validation of computational fluid dynamics methodology used for human upper airway flow simulations. *J Biomech* 2009; **42**: 1553–9. doi: <https://doi.org/10.1016/j.jbiomech.2009.03.035>
- Chen H, Aarab G, de Ruiter MH, de Lange J, Lobbezoo F, van der Stelt PF. Three-dimensional imaging of the upper airway anatomy in obstructive sleep apnea: a systematic review. *Sleep*

Conclusion

The airway resistance during expiration (R_{ex}) is the most relevant characteristic of the airflow in the oropharynx related to the upper airway collapse in OSA patients. Therefore, the repetitive collapse of the upper airway may be explained by the high R_{ex} , which is related to the CSA_{min} of the oropharynx.

- Med* 2016; **21**: 19–27. doi: <https://doi.org/10.1016/j.sleep.2016.01.022>
27. Johnson DM, Soose RJ. Updated nasal surgery for obstructive sleep apnea. *Adv Otorhinolaryngol* 2017; **80**: 66–73. doi: <https://doi.org/10.1159/000470868>
28. Georgalas C. The role of the nose in snoring and obstructive sleep apnoea: an update. *Eur Arch Otorhinolaryngol* 2011; **268**: 1365–73. doi: <https://doi.org/10.1007/s00405-010-1469-7>
29. Lee RW, Chan AS, Grunstein RR, Cistulli PA. Craniofacial phenotyping in obstructive sleep apnea—a novel quantitative photographic approach. *Sleep* 2009; **32**: 37–45.
30. Larsson LG, Lindberg A, Franklin KA, Lundbäck B. Gender differences in symptoms related to sleep apnea in a general population and in relation to referral to sleep clinic. *Chest* 2003; **124**: 204–11. doi: <https://doi.org/10.1378/chest.124.1.204>
31. Brennick MJ, Pack AI, Ko K, Kim E, Pickup S, Maislin G, et al. Altered upper airway and soft tissue structures in the New Zealand Obese mouse. *Am J Respir Crit Care Med* 2009; **179**: 158–69. doi: <https://doi.org/10.1164/rccm.200809-1435OC>
32. Redline S, Kump K, Tishler PV, Browner I, Ferrette V. Gender differences in sleep disordered breathing in a community-based sample. *Am J Respir Crit Care Med* 1994; **149**(3 Pt 1): 722–6. doi: <https://doi.org/10.1164/ajrccm.149.3.8118642>
33. Suratt PM, Dee P, Atkinson RL, Armstrong P, Wilhoit SC. Fluoroscopic and computed tomographic features of the pharyngeal airway in obstructive sleep apnea. *Am Rev Respir Dis* 1983; **127**: 487–92. doi: <https://doi.org/10.1164/arrd.1983.127.4.487>
34. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. *Physiol Rev* 2010; **90**: 47–112. doi: <https://doi.org/10.1152/physrev.00043.2008>
35. Schwab RJ, Geftter WB, Hoffman EA, Gupta KB, Pack AI. Dynamic upper airway imaging during awake respiration in normal subjects and patients with sleep disordered breathing. *Am Rev Respir Dis* 1993; **148**: 1385–400. doi: <https://doi.org/10.1164/ajrccm/148.5.1385>
36. Verbraecken JA, De Backer WA. Upper airway mechanics. *Respiration* 2009; **78**: 121–33. doi: <https://doi.org/10.1159/000222508>
37. Morrell MJ, Arabi Y, Zahn B, Badr MS. Progressive retropalatal narrowing preceding obstructive apnea. *Am J Respir Crit Care Med* 1998; **158**: 1974–81. doi: <https://doi.org/10.1164/ajrccm.158.6.9712107>
38. Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. Physiologic and clinical implications. *Chest* 1990; **98**: 317–24. doi: <https://doi.org/10.1378/chest.98.2.317>
39. Cheng GC, Koomullil RP, Ito Y, Shih AM, Sittitavornwong S, Waite PD. Assessment of surgical effects on patients with obstructive sleep apnea syndrome using computational fluid dynamics simulations. *Math Comput Simul* 2014; **106**: 44–59. doi: <https://doi.org/10.1016/j.matcom.2012.11.008>
40. Ito Y, Cheng GC, Shih AM, Koomullil RP, Soni BK, Sittitavornwong S, et al. Patient-specific geometry modeling and mesh generation for simulating obstructive sleep apnea syndrome cases by maxillomandibular advancement. *Math Comput Simul* 2011; **81**: 1876–91. doi: <https://doi.org/10.1016/j.matcom.2011.02.006>
41. Kim T, Kim HH, Hong S, Baek SH, Kim KW, Suh SH, et al. Change in the upper airway of patients with obstructive sleep apnea syndrome using computational fluid dynamics analysis: conventional maxillomandibular advancement versus modified maxillomandibular advancement with anterior segmental setback osteotomy. *J Craniofac Surg* 2015; **26**: E765–E770. doi: <https://doi.org/10.1097/SCS.0000000000002209>
42. Liu SY, Huon LK, Iwasaki T, Yoon A, Riley R, Powell N, et al. Efficacy of maxillomandibular advancement examined with drug-induced sleep endoscopy and computational fluid dynamics airflow modeling. *Otolaryngol Head Neck Surg* 2016; **154**: 189–95. doi: <https://doi.org/10.1177/0194599815611603>
43. Sittitavornwong S, Waite PD, Shih AM, Cheng GC, Koomullil R, Ito Y, et al. Computational fluid dynamic analysis of the posterior airway space after maxillomandibular advancement for obstructive sleep apnea syndrome. *J Oral Maxillofac Surg* 2013; **71**: 1397–405. doi: <https://doi.org/10.1016/j.joms.2013.02.022>
44. Yu CC, Hsiao HD, Lee LC, Yao CM, Chen NH, Wang CJ, et al. Computational fluid dynamic study on obstructive sleep apnea syndrome treated with maxillomandibular advancement. *J Craniofac Surg* 2009; **20**: 426–30. doi: <https://doi.org/10.1097/SCS.0b013e31819b9671>
45. Van Holsbeke C, De Backer J, Vos W, Verdonck P, Van Ransbeeck P, Claessens T, et al. Anatomical and functional changes in the upper airways of sleep apnea patients due to mandibular repositioning: a large scale study. *J Biomech* 2011; **44**: 442–9. doi: <https://doi.org/10.1016/j.jbiomech.2010.09.026>
46. Mihaescu M, Murugappan S, Gutmark E, Donnelly LF, Kalra M. Computational modeling of upper airway before and after adenotonsillectomy for obstructive sleep apnea. *Laryngoscope* 2008; **118**: 360–2. doi: <https://doi.org/10.1097/MLG.0b013e31815937c1>