A comparison of minimal cross sectional areas, nasal volumes and peak nasal inspiratory flow between patients with obstructive sleep apnea and healthy controls*

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Abstract

Background: The differences in nasal geometry and function between OSA patients and healthy individuals are not known. Our aim was to evaluate the differences in nasal geometry and function using acoustic rhinometry (AR) and peak nasal inspiratory flow (PNIF) between an OSA population and healthy controls.

Methodology: The study was designed as a prospective case-control study. Ninety-three OSA patients and 92 controls were enrolled from 2010 – 2015. The minimal cross-sectional area (MCA) and the nasal cavity volume (NCV) in two parts of the nose (MCA_{0-3}/NCV_{0-3} and $MCA_{3-5.2}$/$NCV_{3-5.2}$) and PNIF were measured at baseline and after decongestion.

Results: The mean MCA_{0-3} in the OSA group was 0.49 cm^2 compared to 0.55 cm^2 in controls ($p < 0.01$, 95% CI [-0.10, -0.02]). The mean NCV_{0-3} correspondingly was 2.51 cm^3 compared to 2.73 cm^3 in controls ($p < 0.01$, 95% CI [-0.37, -0.08]). PNIF measured 105 litres/minute in the OSA group and 117 litres/minute in the controls ($p < 0.01$, 95% CI [-21.8, -3.71]).

Conclusions: OSA patients have a lower minimum cross-sectional area, nasal cavity volume and peak inspiratory flow compared to controls. Our study supports the view that changes in the nasal cavity may contribute to development of OSA.

Key words: nasal cavity, sleep apnea syndromes, nasal surgical procedures, rhinometry, and continuous positive airway pressure

Introduction

In obstructive sleep apnea (OSA) nasal continuous positive airway pressure devices (nCPAP) remains the preferred treatment, despite various surgical procedures evolving during the last three decades [1]. The use of nCPAP treatment requires a functional nasal cavity in order to work adequately, and nasal surgery may be needed to reduce nasal resistance [2]. When applying the Sher criteria for surgical success of OSA [3, 4], 15 – 17% of patients with nasal obstruction will benefit from nasal surgery as a primary treatment. In some cases nasal surgery is reported to increase the number of apnea and hypopneas [3] and to induce central apnoea [4]. There are studies that suggest a connection between nasal patency and OSA [5], and a study by Lofaso [6] has shown increased nasal resistance in patients with OSA compared to controls. Still, little is known about potential differences in nasal geometry and function between OSA patients and healthy individuals. The primary aim of this study was to compare objective measures of minimal cross-sectional area (MCA), nasal cavity volume (NCV) and peak nasal inspiratory flow (PNIF) between patients with OSA and a group of healthy individuals. The secondary aim was to evaluate possible differences in the nasal congestion index (NCI).

Materials and methods

The study was designed as a prospective case-control trial and was approved by the Norwegian Regional Committee for Medi-

cal Research Ethics (REK) and was registered in Clinicaltrials.gov (NCT01282125). Ninety-three patients with verified OSA and 92 normal controls aged > 18 years and < 75 years were included in the period 2010 to 2015 from two tertiary medical centres in central Norway. The patients were selected from Aleris Hospital in Trondheim, Norway and the controls were selected randomly both from the outpatient clinics at Aleris Hospital and the ENT department, St. Olavs University Hospital. The controls were hospital workers or workers outside of the hospital included from annual controls as part of their mandatory occupational health service check ups. Registered nurses were in charge of the selection and were blinded in regards to information on upper airway examinations. Written informed consent was obtained from all patients and controls prior to inclusion in the trial. Inclusion criteria in the patient group were OSA, verified with a portable sleep polygraph, no prior nasal surgery and no use of nasal steroids or nasal decongestion the last three months prior to inclusion, and no clinical evidence of nasal polyposis. The OSA group was referred to the hospital from general practitioners, ENT specialist or pulmonary specialist in central Norway. Inclusion criteria in the control group were no prior nasal surgery, no use of nasal steroids or nasal decongestion the last three months prior to inclusion, no clinical evidence of nasal polyposis and no complaints of daytime drowsiness, excessive snoring or observed apneas by others.

Method

All patients underwent a portable sleep polygraph to verify the OSA diagnosis (Embletta Diagnostic System, ResMed, San Diego, CA, USA, and Nox Medical T3, ResMed, Reykjavík, Iceland). Apnea was scored when there was a drop in the peak signal by ≥ 90% of pre-event baseline using an oronasal sensor for ≥ 10 seconds. Hypopnea was scored when the peak signal dropped by ≥ 30% of pre-event baseline using nasal pressure for ≥ 10 seconds in association with ≥ 3% arterial oxygen desaturation. An apnea-hypopnea-index (AHI) > 5 per hour was considered abnormal. An experienced sleep physiologist examined the results manually to ensure the diagnosis. Both patients and controls were then subjected to an outpatient examination using acoustic rhinometry (AR) to obtain geometrical data in the nose, and peak nasal inspiratory flow (PNIF) to measure the maximum forced inspiration. None of the OSA patients were subject to CPAP treatment prior to the tests, although some had their initial adjustment and fitting of the masks in advance.

Acoustic rhinometry (AR)

AR was performed measuring the minimal cross-sectional area (MCA) and nasal cavity volume (NCV) in two areas of the nasal cavity. AR utilizes a sonographic technique and all measurements were made with an acoustic rhinometer (Rhinometrics SRE2100, Rhinoscan version 2.5, built 3.2.5.0; Interacoustics, Minneapolis, MN, USA). Three trained operators made the measurements with the subjects sitting opposite to the investigator using a handheld probe and a nose adaptor. Sufficient contact between the adaptor and the nose was secured using contact gel, and the average of three satisfactory recordings was obtained. The rhinometer calculated the cross sectional area and volume in two parts of the nose. The most anterior part was defined as 0 – 30 mm measured from the nostrils, and the posterior part 30 – 52 mm from the nostrils, defining the MCA0-3/ NCV0-3 and MCA3-5.2/ NCV3-5.2 areas respectively, a classification previously described by Kjærgaard and Steinsvåg in 2009 [7]. Measurements were obtained at baseline and 15 minutes after decongestion of the nasal mucosa with topical xylometazoline (Otrivin® 1 mg/ml, Novartis, Basel, Switzerland). The total nasal cavity volume ($NCV_{0-5.2}$) was calculated from the combined values of NCV_{0-3} and $NCV_{3-5.2}$. Sixteen patients were excluded due to inadequate AR measurements.

Peak nasal inspiratory flow (PNIF)

The maximal nasal inspiratory flow was measured using a portable PNIF meter (in-check DIAL; Clement Clarke International, Harlow, Essex, UK). The mean of three approved PNIF measurements was recorded with the subjects in a sitting position and the head held in a level position. PNIF was obtained before AR was performed, and both procedures were repeated after decongestion. One control was unable to perform PNIF.

Nasal congestion index (NCI)

The nasal congestion index was obtained to evaluate the swelling of nasal mucosa. We used the following formula: [decongested value – baseline value]/ baseline value. NCI was calculated for the following values: MCA_{0-3}, $MCA_{3-5.2}$, NCV_{0-3}, $NCV_{3-5.2}$ and $NCV_{0-5.2}$.

Statistics

All data showed a normal distribution and are reported as mean values with standard deviation (SD) and 95% confidence intervals (95% CI). An independent sample t-test was used to compare the mean values. The p-value was considered significant if $p < 0.05$. We considered a difference of 0.05 cm^2 in MCA_{0-3} as a clinically significant difference between the groups, which is slightly lower than the mean difference in MCA in this study (0.06 cm^2) and equal to the mean difference in MCA in similar studies [8]. In order to prove this difference with a level of significance set at 0.05 and strength of 0.80, we needed 91 subjects in each group. A multivariate linear regression analysis was used to adjust for the possible confounding of bodyweight and BMI. We did not conclude with a strong dependency on age upon the outcome of AHI and we did not include age in the multivariate analysis. SPSS, version 23 for Mac, was used for the statistical analysis (SPSS Inc., Chicago, IL, USA).

Table 1. Patient demographics.

	OSA (N=93)	Controls (N=92)	P
Gender Female (%) Male (%)	 25 (26,9) 68 (73,1)	 23 (25,0) 69 (75)	 0.77
Mean age, years (range)	49.3 (27-72)	46.0 (20-69)	0.06
Mean height , m (SD)	1.77 (0.10)	1.78 (.09)	0.40
Mean weight, kg (SD)	95.4 (16.7)	82.4 (14.6)	<0.01
Education, years (%) <9 10-12 >13	 12 (12.9) 28 (30.1) 53 (57.0)	 12 (13.0) 24 (26.1) 56 (60.9)	0.72
Disease, n (%) Heart disease Allergy	 9 (9.7) 17 (18.3)	 8 (8.7) 10 (10.9)	 0.80 0.15
Mean BMI, kg/m^2 (SD)	30.3 (4.3)	25.8 (3.5)	<0.01

Results

Table 1 shows the baseline data in both groups. The mean AHI in the OSA group was 31.22 (9.0 - 93.3). The distance from the nasal orifice to the lowest value of MCA was in both cases coinciding with MCA_{0-3}, and was not statistically different in the groups (1.90 cm in the OSA group and 1.86 cm in the control group, p > 0.10).

MCA and NCV

MCA_{0-3}, $MCA_{3-5.2}$ and NCV_{0-3} were significantly lower in the OSA group at baseline. In addition, $NCV_{3-5.2}$ and $NCV_{0-5.2}$ differed significantly from the control group after decongestion (Table 2). When analysing the covariates of weight and BMI, we found that these variables did not significantly predict MCA_{0-3} in the OSA group (F (2,90) = 1,10, p= 0.34, R2 = .024) nor NCV_{0-3} (F (2,90) = 3,00, p =0.06 R2 = .062).

PNIF

PNIF was significantly lower in the OSA group compared to the controls both at baseline and after decongestion (Table 2). The change in PNIF (delta PNIF = PNIF after decongestion – PNIF before decongestion) was also lower in the OSA group compared to the controls (Figure 1).

NCI

NCI was significantly lower in the patient group for volume in the anterior part and for the total nasal volume, but not for MCA_{0-3}, nor for $MCA_{3-5.2}$ or $NCV_{3-5.2}$ (Table 3).

Subgroup analysis

OSA was classified as mild (AHI < 15, n = 16), moderate (AHI 15 – 29.9, n = 36) and severe (AHI > 30, n = 41). In the subgroup analysis MCA_{0-3} and NCV_{0-3} were significantly smaller ($p < 0.05$) in patients with mild and severe OSA both at baseline and after decongestion compared to the controls. The moderate OSA group showed significantly smaller MCA_{0-3} and NCV_{0-3} only after decongestion compared to the controls ($p<0.05$).

Discussion

This study demonstrates a significantly smaller cross sectional area and smaller nasal cavity volume in OSA patients than in controls. The difference between the groups is greater in the anterior part of the nose, from 0–3 cm and is enhanced after decongestion. This can support the idea of a more profound anatomical deviation in OSA patients in the area of the nasal vestibulum, anterior part of the nasal septum and inferior turbinates, commonly referred to as the nasal valve area. Another explanation for the smaller nasal cavity in OSA patients could theoretically be hypoplasia of the nasal cavity due to lack of function over time, with a predominant oral breathing instead of nasal breathing. A parallel to this development can be seen in asthmatics where lung function is decreased when nasal

Table 2. Minimum cross sectional area, nasal cavity volume and peak nasal inspiratory flow at baseline and after decongestion.

	Before decongestion				After decongestion			
	OSA (N=93)	Controls (N=92)	P	95% CI	OSA (N=93)	Controls (N=92)	P	95%CI
MCA_{0-3}	0.49 (0.14)	0.55 (0.13)	<0.01	(-.10, -.02)	0.54 (0.13)	0.60 (0.14)	<0.01	(-.10, -.02)
$MCA_{3-5.2}$	0.95 (0.40)	1.08 (0.41)	0.03	(-.25, -.01)	1.29 (0.48)	1.60 (0.53)	<0.01	(-.45, -.16)
NCV_{0-3}	2.51 (0.47)	2.73 (0.53)	<0.01	(-.37, -.08)	2.62 (0.49)	2.95 (0.54)	<0.01	(-.48, -.18)
$NCV_{3-5.2}$	3.41 (1.25)	3.57 (1.34)	0.43	(-.52, .22)	4.83 (1.31)	5.49 (1.64)	<0.01	(-1.09, -.23)
$NCV_{0-5.2}$	5.91 (1.54)	6.30 (1.75)	0.12	(-.85, .10)	7.46 (1.64)	8.45 (2.04)	<0.01	(-1.53, -.46)
PNIF	105 (25)	117 (36) (N=91)	<0.01	(-21.8, -3.71)	113 (20)	129 (46) (N=91)	<0.01	(-26.3, -5.68)

MCA = minimum cross sectional area; NCV = nasal cavity volume, PNIF = peak nasal inspiratory flow. Data presented as mean (SD) and 95% confidence interval (95% CI).

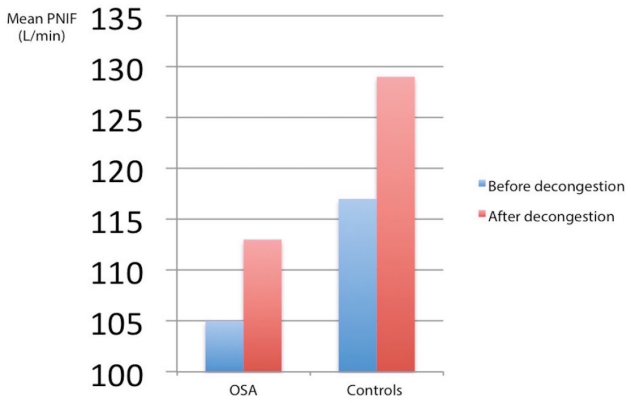

Figure 1. Peak nasal inspiratory flow (PNIF) at baseline and after decongestion in obstructive sleep apnea patients (OSA) and controls. There is a significant difference in PNIF between the groups both at baseline (blue column, $p < 0.01$) and after decongestion (red column, $p < 0.01$).

Table 3. Nasal congestion index for minimum cross sectional area and nasal cavity volume.

	OSA (N=93)	Controls (N=92)	P	95%CI
NCI-MCA_{0-3}	0.13 (0.22)	0.09 (0.17)	0.19	(-.02, .09)
NCI-$MCA_{3-5.2}$	0.48 (0.78)	0.56 (0.43)	0.36	(-.27, .10)
NCI-NCV_{0-3}	0.054 (0.10)	0.09 (0.11)	0.03	(-.07, -.004)
NCI-$NCV_{3-5.2}$	0.53 (0.57)	0.62 (0.39)	0.17	(-.24, .04)
NCI-$NCV_{0-5.2}$	0.29 (0.26)	0.37 (0.23)	0.03	(-.15, -.006)

NCI = nasal congestion index, MCA = minimum cross sectional area, NCV = nasal cavity volume. Data presented as mean (SD) and 95% confidence interval (95% CI).

breathing is obstructed [8,9] and in laryngectomy patients up to two years after surgery [10]. In both studies MCA and NCV were found to be smaller in the diseased group compared to controls. Further, the PNIF values were significantly lower in the OSA group. The most likely reason for this is the smaller MCA_{0-3} in the patient group. The difference in MCA and NCV between the groups is confined mostly in the nasal valve area, which is the site of most resistance in the upper airway [11]. The nasal valve is made up of the upper crest of the nasal septum and the upper lateral cartilage, the bony entrance to the nasal cavity, the inferior turbinate and the length of the erectile septal body [12]. A slight decrease in the radius in this area will have a large negative impact on the flow rate according to Poiseuilles law which states that the volume flow rate is dependent upon the radius raised to the fourth power [13]. It is therefore likely that even small changes in nasal architecture in the nasal valve will be a limiting factor for the airflow downstream. Even though we demonstrated that BMI did not contribute significantly to the prediction of PNIF, a reduction in lung function is correlated to a lower forced inspiratory flow as demonstrated in patients with obstructive pulmonary disease [8]. There is also the possibility that the reduced PNIF values in OSA patients is due to a second obstructive site downstream in the oro-or hypopharynx or an inadequate contraction of the pharyngeal dilator muscles as explained by the nasal ventilatory reflex mechanism [14]. A relative obstruction during inspiration could be caused by enlarged pharyngeal tissue, an enlarged tongue base with posterior displacement of the epiglottis, or enlarged tonsils. Senchak et al. demonstrated the latter where adult tonsillectomy in young, overweight males with a median Friedman stage of 3 was clearly beneficial in OSA treatment [15]. The lack of proper nasal ventilatory reflex mechanisms was demonstrated by McNicholas et al. in a study where anaesthesia of the nasal mucosa induced an increased upper airway obstruction [14]. Others have demonstrated that concentration of nasal nitric oxide (NO), a potent vasodilator in the lungs, is dependent on airflow [16] and that reduction of inhaled NO can alter the ventilation-perfusion ratio in the lungs and thus might influence the inspiratory flow [17]. In addition to significantly lower PNIF value in the OSA group, the present study also demonstrates a lower increase in PNIF after decongestion in the OSA group compared to controls. Although the difference in increase of PNIF is not statistically significant, it does reflect the reduced capacity of forced inhalation in OSA patients even after decongestion of the nose. This may either be viewed as a fundamental characteristic of OSA, or as a fundamental trait of decongestion itself in OSA patients. NCI values for both NCV_{0-3} and $NCV_{0-5.2}$ showed a significant lower value in the OSA group reflecting a lower mucosal congestion compared to the higher reversible congestion in controls (Table 3). We did not find any significant reduction of NCI values for MCA, only for NCV in the anterior part. Since the use of topical xylometazoline will reduce mucosa by vasoconstriction alone [18], this is an indication of additional factors causing narrowing or mucosal oedema in OSA patients. We can suggest three possible explanations. There might be inflammatory responses in OSA [19] that are not subject to nasal decongestion in the same way as non-OSA subjects. As a continuation of this idea, there might be a dysfunction in the relatively newly described mucosal regulation by particular classes of neuropeptides [20]. A rise in expired CO_2, as seen in periods with prolonged apnea, can possibly interact with mucosal sensory neurons, some of which contain calcitonin gene related peptide (CGRP) which regulates arterial and arteriovenous vessels beneath the epithelial basement membrane [21,22] and are not involved in the regulation of the venous sinusoids. A third explanation could be that the bony anatomy of the inferior turbinate in OSA patients differs from the controls.

A smaller distance between the inferior turbinate and nasal septum will thus explain less decongestion of the mucosa in the OSA patients. This explanation can be supported of an earlier trial where we demonstrated that OSA patients improved after septoplasty when inferior turbinate reduction was incorporated in the procedure [23].

However, a larger nasal cavity in which the airflow is restored in a more laminar fashion, for instance after septal or volume-reductive surgery, does not mean that OSA patients will be relieved of apneas. In the literature there are examples of intranasal surgeries that lead to an increase in apneas in some patients [3, 4]. We can hypothesize that some of the negative effect can be mechanical, due to a larger input of flow downstream, and hence a larger suction force in the collapsible segment in the hypopharynx. In a starling resistor model there would be a collapsible segment in the pharynx and collapse occurs when the critical pressure in the pharynx is greater than the pressure in the rigid inlet area (the nose). If the inlet pressure drops after surgery, it might become lower than the pressure in the pharynx leading to a collapse [24]. Recent publications by Owens et.al have demonstrated that the Starling resistor model is insufficient in predicting nasal airflow alone [25]. It might be possible that intranasal surgery interferes with the neuroregulatory mechanisms in such a way that it inhibits the proper response in the dilator muscles of the throat. The central apnea that sometimes can be observed after successful intranasal surgery [4] is most likely due to the same mechanisms that causes the complex OSA seen when introducing CPAP therapy in selected cases; a ventilatory decrease in CO2 and a loss of the central respiratory drive [26].

Limitations of the study

One cannot rule out the possibility that some subjects in the control group might have OSA, since they did not undergo a sleep polygraph. However, exclusion of these controls would strengthen the differences rather than weaken them. There is also a possibility that the OSA group to some extent could be biased in the sense that ENT specialists, who might be more focused on nasal obstruction than general practitioners or pulmonary specialists, referred a larger proportion of this group to sleep polygraphy. This is, however, not different from usual clinical practice where patients are referred mainly from ENT specialists to sleep polygraphy. We have not performed any analysis of variations due to seasonal changes, but the inclusion period spanned several years, which would minimize possible bias due to pollen season or wintertime.

Conclusion

Compared to a healthy population the nasal cavity is smaller in OSA patients, and the difference is greatest at the site of the nasal valve area. A reduced response to decongestion in the OSA group indicates a larger bone to mucosa ratio of the anterior part of the inferior turbinate or an inflammatory cause of mucosal oedema. The resulting smaller inlet area of the nose is a probable cause of the reduction in peak nasal inspiratory flow in OSA patients compared to controls. This study supports the view that a narrow nose may contribute to development of OSA but it is still unclear how a smaller nasal cavity contributes to changes in airway collapse.

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Authorship contribution

MHSM has written the main text and collected the data in both groups and been in charge of the statistical analysis, tables and figures. VB has been a co-author and helped in the design and text work, tables and figures. WMT has been a co-author and helped in text work and in collection of parts of the control group. SN has been in charge of the supervision of collection of data, helped in the design and the text work. GB has helped in the text work related to the analysis of sleep recordings.

Conflict of interest

To our knowledge, there is no conflict of interest.

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