



Nasal flow, volumes, and minimal cross sectional areas in asthmatics



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Summary

Background: The Unified Airways hypothesis suggests an involvement of the upper airways in asthma. Critical parameters of the nasal airway can be quantified objectively with acoustic rhinometry (AR) and peak nasal inspiratory flow (PNIF).

Objective: We aimed to investigate nasal airway patency in asthmatics compared to non-asthmatic controls. Nasal volume, cross sectional area and flow were measured using acoustic rhinometry (AR) and peak nasal inspiratory flow (PNIF) in 87 asthmatics and 93 non-asthmatic controls before and after decongestion with xylometazoline. Nasal congestion index (NCI) was calculated, and allergy status was assessed by skin prick test or specific IgE.

Results: We found significantly smaller minimum cross sectional area and nasal cavity volume in asthmatics than controls, and the cross sectional area is at its minimum at 2–3 cm from the nasal orifice in both groups. AR and PNIF measurements are not different in allergic and non-allergic subjects in either group. The effect of xylometazoline is not significantly different between the 2 groups with regard to AR, but there is a significant improvement in PNIF for the asthmatics when assessed by the NCI.

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Conclusion: The present study demonstrates a significantly smaller nasal airway when assessed by minimum cross sectional area and nasal cavity volume in asthmatics than controls, and these findings apply to asthmatics and controls irrespective of allergy status.

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Introduction

The Unified Airways hypothesis suggests an involvement of the upper airways in asthma [1–3]. Rhinitis typically precedes the development of asthma and can contribute to unsatisfactory asthma control. Nasal symptoms, airflow, and markers of inflammation directly correlate with lower airway involvement [4]. In both rhinitis and asthma, an inflammatory cell infiltrate with subepithelial oedema is present in the mucosa [5]. Unlike the lower airway, the nasal mucosa contains venous sinusoids that undergo periodic congestion and decongestion (the nasal cycle) that are important for regulation of airflow, humidification and warming of the inspired air. Nasal obstruction may be indicative of structural deformities, infections and inflammatory conditions in the nose, and is frequently reported by asthmatics [6]. Their lack of nasal patency may also be due to factors such as mucosal congestion and changed perception of flow.

Critical parameters of the nasal airway can be quantified objectively with acoustic rhinometry (AR) and peak nasal inspiratory flow (PNIF) [7,8]. While the former measures internal nasal volume and minimum cross-sectional areas, the latter measures the maximum nasal inspiratory flow during forced inspiration. The Nasal Congestion Index (NCI) has been suggested as a useful instrument for the evaluation of nasal obstruction by quantifying the effect of topical decongestants applied on the nasal mucosa [9]. There are few studies that have used these tools to investigate the relative contribution of subepithelial oedema and congestion of the venous sinusoids in asthmatics. Hellgren et al. [10] demonstrated increased nasal mucosal swelling in asthmatics compared to healthy controls.

In this study, we measured nasal volume, cross sectional area and flow using AR and PNIF, and assessed the effect of xylometazoline using the NCI in order to further elucidate the role of oedema and congestion in the nasal mucosa of asthmatics.

Methods

Subjects

The study consisted of 87 patients with asthma, and they were recruited from the out-patients' clinic at the Department of Lung Medicine, St Olavs Hospital, University Hospital of Trondheim. The asthma diagnosis was based on the presence of typical asthma symptoms, with either $\geq 12\%$ and ≥ 200 ml improvement of forced expiratory volume in the first second (FEV₁) from baseline after inhalation of salbutamol or positive methacholine bronchial provocation test (PD20 FEV₁ ≤ 1600 μg) and in accordance with the British Thoracic Society criteria [11].

Ninety-three non-asthmatic controls were mostly recruited from the out-patients' clinic of Department of Otolaryngology, Head and Neck Surgery, St Olavs Hospital, University Hospital of Trondheim, among patients with disorders not affecting the upper airways (e.g. external otitis, and skin diseases in the ENT area). Some controls were also randomly invited from nearby businesses with all types of employments, from manual labour to skilled work. The sample, allergy status, questionnaires and additional recordings were based on a database that has previously been described [6]. Exclusion criteria were the presence of acute and chronic rhinosinusitis and nasal polyposis on oto-rhino-laryngological examination and in accordance to the EPOS 2012 criteria [12], pregnancy, previous nasal surgery, systemic disease with potential affection of the nose, such as Wegener's granulomatosis, cystic fibrosis, primary ciliary dyskinesia, Kartagener's syndrome and sarcoidosis, and a history of cancer. For the NCI we analyzed 85 patients with asthma and 93 non-asthmatic controls. The missing values were discarded because of one patient with missing decongested values and one patient was resistant to accept topical xylometazoline. The study was approved by the Regional Committee for Medical Research Ethics, and conducted according to the Helsinki Declaration. Written informed consent was obtained.

AR

AR is a sonic echo technique which was used to measure the nasal volumes and minimal cross sectional areas. Nasal passage volumes are calculated from contiguous cross-sectional values.

The measurements were made with an impulse acoustic rhinometer (RhinoMetrics SRE2100, RhinSCAN version 2.5, built 3.2.5.0; Interacoustics, Minneapolis, MN) by two trained operators throughout the study. The probe was hand held with the subject sitting upright and opposite to the investigator. An appropriate anatomic nose adaptor and contact gel between the nose adaptor and the nostril were used, and measurements were made during a breath hold.

Recordings were performed according to published protocols [13]. Briefly, three satisfactory recordings were made from each nasal cavity. The values for each nasal cavity were averaged. Due to the variations represented by the nasal cycle, the sum of the two averages was divided by 2 to obtain the minimal cross sectional area (MCA, cm^2) and nasal cavity volume (NCV, cm^3). The rhinometer was programmed to calculate the MCA_{0–3} and MCA_{3–5.2}, and NCV_{0–3} and NCV_{3–5.2}, defined as MCA and NCV at 0–3 cm and 3–5.2 cm, respectively from the nasal orifice. MCA_{0–5.2} is the minimum cross sectional area at 0–5.2 cm from the nasal orifice. NCV_{0–5.2} is the sum of NCV_{0–3} and NCV_{3–5.2}.

After visual inspection of the rhinometric curves, the rhinometer was reprogrammed to calculate MCA_{0–2} and

MCA_{2-4} , and NCV_{0-2} and NCV_{2-4} , defined as 0–2 and 2–4 cm, respectively from the nasal orifice. MCA_{0-4} is the minimum cross sectional area at 0–4 cm from the nasal orifice. NCV_{0-4} is the sum of NCV_{0-2} and NCV_{2-4} .

PNIF

Peak nasal inspiratory flow was assessed with a portable PNIF meter (In-check DIAL; Clement Clarke International, Harlow, Essex, UK). The average of three satisfactory maximal nasal inspirations with the patient in the sitting position was recorded.

Maximum flow registration was limited to 120 l/min. Peak flows exceeding 120 l/min were recorded as 120 l/min.

Nasal decongestion

After baseline recordings of AR and PNIF, the nasal mucosa was decongested with two sprays of topical xylometazoline (OtrivinVR 1 mg/ml, Novartis, Basel, Switzerland) applied in a standardized manner with a hand pump to each nasal cavity. Recordings of AR and PNIF were repeated after 10 min.

NCI

The effect of topical xylometazoline on MCA, NCV and PNIF was assessed by calculating the Nasal Congestion Index [9] for each variable using the following equation: $NCI = (\text{post xylometazoline value} - \text{baseline value}) / \text{baseline value}$.

A low NCI indicates minor mucosal congestion as opposed to a high NCI which suggests a high degree of reversible mucosal congestion.

Allergy

Sensitization to house dust mite, cat, dog, horse, timothy grass and birch pollens, mugwort and cladosporium was assessed with either specific IgE measurement (AlaTOP, Diagnostic Products Corporation, Los Angeles, California, USA) or skin prick tests (Soluprick SQ, ALK-Abello, Hørsholm, Denmark). Antihistamines were discontinued 4 days prior to skin prick tests. Subjects with typical symptoms of hypersensitivity on exposure to the allergen(s) and positive tests were classified as allergic.

Statistics

The data were tested for normal distribution using normal probability plots and presented as mean, standard

deviation (SD) or 95% confidence interval (95% CI). The independent samples *t* test was used to evaluate differences in mean values in the asthmatic and control groups. Analysis of variance (ANOVA) with the post hoc application of Bonferroni correction was used to assess the effect of allergy status in both asthma and control groups. A *P*-value of <0.05 was considered to be statistically significant.

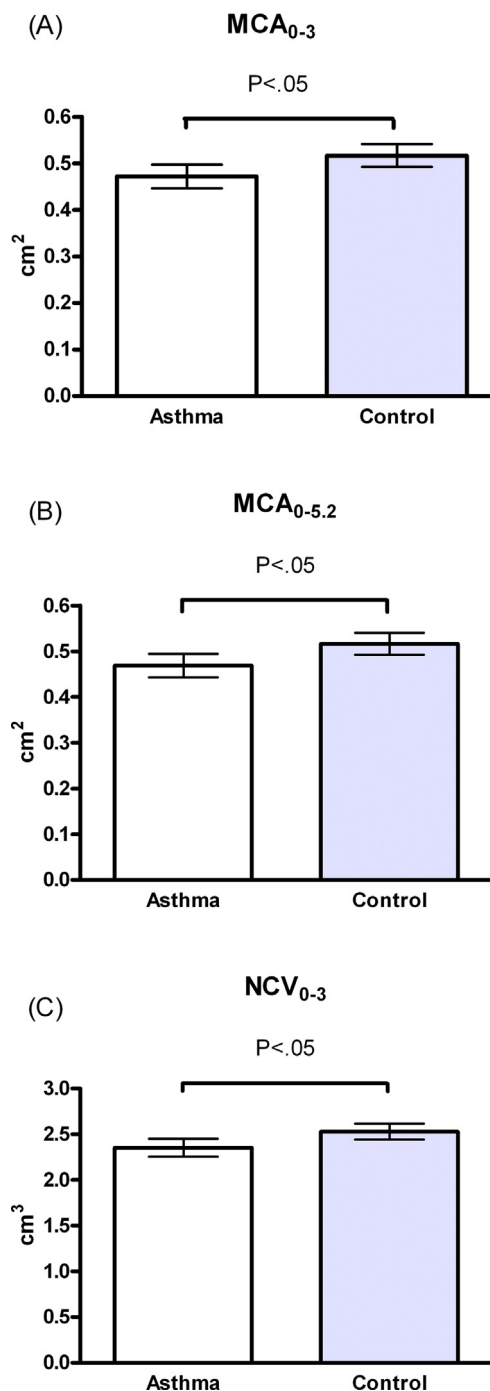


Figure 1 MCA_{0-3} (A), $MCA_{0-5.2}$ (B) and NCV_{0-3} (C) in the asthmatic patients (white bars) and controls (grey bars). Values presented as mean, 95% CI. Abbreviations: MCA = minimum cross sectional area; NCV = nasal cavity volume; $_{0-3}$ = 0–3 cm behind the nasal orifice; $_{0-5.2}$ = 0–5.2 cm behind the nasal orifice.

Table 1 Patient demographics.

	Asthmatics, <i>N</i> = 87	Controls, <i>N</i> = 93
Mean age, years (range)	43.7 (19–64)	44.0 (20–65)
Mean BMI, kg/m ² (SD)	26.8 (5.0)	25.2 (3.3)
Gender, Male, <i>n</i> (%)	36 (41)	41 (44)
Allergy, <i>n</i> (%)	52 (60)	20 (22)
Smoking, <i>n</i> (%)	9 (10)	12 (13)

All statistical analyses were performed using PASW Statistics, version 18 for Windows (SPSS Inc., Chicago, IL, USA).

Results

The demographic data are presented in Table 1. The mean (95% CI) baseline FEV₁ was significantly lower in asthma patients than controls [2.79 (2.61–2.97) vs 3.46 (3.26–3.65) l, $P < 0.001$].

Rhinometry measurements

Data on rhinometric variables at baseline and after topical xylometazoline, calculated as the NCI, are presented in Table 2.

MCA_{0–3}, MCA_{0–5.2} and NCV_{0–3} were significantly lower in asthmatics than in controls (Fig. 1). In the asthma group the MCA for the whole nasal airway (MCA_{0–5.2}) was located in the anterior region (MCA_{0–3}) in 95% and more posteriorly (MCA_{3–5.2}) in 5% of subjects. In the control group the MCA_{0–5.2} was located in the anterior region (MCA_{0–3}) in 98% and more posteriorly (MCA_{3–5.2}) in 2% of the subjects. MCA_{0–2}, MCA_{2–4}, MCA_{0–4} and NCV_{0–2} were significantly lower in asthmatics than in controls (data not shown). The lowest value of the MCA was located at 2–4 cm from the nasal orifice in 59 and 61% of asthmatics and controls, respectively.

NCI was not significantly different between the groups.

Inspiratory flow

The mean (95% CI) PNIF was significantly lower in the asthma group compared to the control group [84 (78–89) vs 102 (98–106) l/min, $P < 0.001$].

The effect of xylometazoline was significantly greater in asthmatics than in controls (Table 2).

Allergy

AR variables and PNIF were not significantly different in asthmatics and controls when analyzed by allergy status (Fig. 2).

Discussion

This study demonstrates that the nasal airway, when assessed by cross sectional area and volume, is significantly smaller in asthmatics than controls, and that the cross sectional area is at its minimum at 2–3 cm from the nasal orifice in both groups. The NCI with regard to AR measurements is not significantly different between the two groups, but there is a significant improvement in NCI for PNIF in the asthmatics. AR and PNIF measurements are not significantly different in allergic and non allergic subjects in either group.

MCA and NCV in asthmatics have been studied previously by two other groups [10,14]. Our finding of a lower MCA at 0–4 cm and NCV at 0–3 cm is in accordance with that of Hellgren et al. They found a decrease in the cross-sectional area at 4 cm and in the volume between 3.3 and 4 cm in the asthma group compared with healthy controls. In contrast, Wålinder et al. did not find any significant difference in minimum cross sectional area and intranasal volume measured between 0 and 5.2 cm in 41 asthmatics and healthy controls.

The location of the MCA in both asthmatics and controls appears to correspond with the location of the internal nasal valve. The latter consists of 4 distinct compartments of airflow resistors: two structural – the cartilaginous termination of the nasal vestibule and the bony entrance to the cavum, and two mucovascular compartments – the inferior turbinate and the septal erectile body, both characterised by numerous venous sinusoids [15]. The magnitude of airflow is determined by the shape and dimensions of these anatomical–physiological narrowings and by airflow velocity [16]. In the present study, it is unlikely that the reduced nasal patency in asthmatics is due to congestion of the venous sinusoids. The decongestive effect of xylometazoline is achieved by vasoconstriction of the nasal venous sinusoids via stimulation of α -2 receptors [17], and there was no significant difference in the NCI for MCA and NCV between the two groups. Thus, the most likely explanation for the differences in nasal patency is the presence of an inflammatory cell substrate, subepithelial oedema and fibrous tissue in those with asthma which is not influenced by decongestive measures. Nasal mucosal inflammation with eosinophilic infiltration has been reported in

Table 2 Acoustic rhinometry and peak nasal inspiratory flow recordings at baseline and nasal congestion index.

Measurement level	Acoustic rhinometry			Nasal congestion index		
	Asthmatics (N = 87)	Controls (N = 93)	P	Asthmatics (N = 85)	Controls (N = 93)	P
MCA _{0–3}	0.47 (0.12)	0.52 (0.12)	0.01	0.12 (0.18)	0.09 (0.17)	0.17
MCA _{3–5.2}	0.89 (0.35)	0.92 (0.27)	0.57	0.65 (0.47)	0.67 (0.43)	0.77
MCA _{0–5.2}	0.47 (0.12)	0.52 (0.12)	<0.01	0.13 (0.19)	0.09 (0.17)	0.10
NCV _{0–3}	2.35 (0.46)	2.53 (0.42)	<0.01	0.09 (0.10)	0.09 (0.10)	0.74
NCV _{3–5.2}	2.95 (1.16)	2.97 (0.88)	0.89	0.43 (0.47)	0.43 (0.34)	0.95
NCV _{0–5.2}	5.30 (1.45)	5.50 (1.20)	0.32	0.25 (0.24)	0.26 (0.19)	0.65
PNIF	84 (24.4)	102 (18.8)	<0.001	0.14 (0.20)	0.06 (0.11)	<0.01

Data presented as mean (SD). Abbreviations: MCA = minimum cross sectional area; NCV = nasal cavity volume; NCI = nasal congestion index; SD = standard deviation; 0–3 = 0–3 cm behind the nasal orifice; 3–5.2 = 3–5.2 cm behind the nasal orifice; 0–5.2 = 0–5.2 cm behind the nasal orifice; PNIF = peak nasal inspiratory flow.

asthmatic subjects without rhinitis [18]. There are conflicting results concerning structural changes such as basal membrane thickening in the nasal mucosa of patients with asthma [19,20]. Other structural factors that may represent a difference are nasal polyps, CRS, previous nasal surgery and chronic immunological/inflammatory conditions, but subjects with these abnormalities were excluded from the present study.

Nasal airway patency depends on the geometry of the airway, airflow and resistance. According to Poiseuille's law flow is directly proportional to the difference in pressure multiplied by the radius raised to the fourth

power. A minimal decrease in the radius of the nasal airway will thus result in a significant reduction in flow [21], illustrated in this study by a reduced MCA and a consequently reduced PNIF in the asthma group. In constricted areas, velocity increases and a relatively negative pressure is generated [21]. These phenomena are seen in the internal nasal valve which represents the flow-limiting region or the bottle-neck area of the nasal cavity. Although the relative changes in NCI MCA in the asthmatic and control groups are equal the MCA in the asthma group is still smaller and this may explain the persistent difference in PNIF after decongestion. In addition to structural and mucosal characteristics, other factors may control nasal airflow. A reduction in forced inspiration may give a reduced stimulation of the sensors for nasal airflow. When the breathing effort is sub maximal or intrapulmonary dynamic resistance is increased, reduced PNIF can give a misleading impression of nasal obstruction. It has also been suggested that asthmatics generally may just have a different subjective perception of nasal obstruction that may explain their oronasal breathing [22].

Breathing is a dynamic process, with turbulent and laminar flow occurring simultaneously in different parts of the nasal passage. AR is static in nature and thus has limitations with regard to detecting dynamic changes. On the other hand, PNIF is effort dependent, but the non-rigidity of the ala nasi may induce dynamic collapse in the compliant part of the external nose. Despite a maximum limitation of PNIF recordings to 120 l/min, we demonstrated highly significant differences between asthmatics and controls. In addition, PNIF values above 120 l/min are only of minor clinical interest because such high peak flows generally exclude nasal obstruction [23,24].

We found that both allergic and non-allergic asthmatics have significantly smaller $MCA_{0-5.2}$ and NCV_{0-3} compared to their respective controls. Other studies have reported that both allergic and non-allergic asthma patients had more nasal symptoms and mucosal abnormalities in the nose and had elevated levels of inflammatory markers in nasal secretions, together with a significant impairment of quality of life and reduced inspiratory nasal airflow compared to non-asthmatics [4,6]. This highlights the importance of a thorough oto-rhino-laryngological examination and evaluation in all asthma patients, beyond the scope of allergy.

As alterations in nasal cavity geometry and airflow may compromise lung function, the results of the present investigation indicate a need for nasal biopsy studies in asthmatics to further understand nasal obstruction in these patients. It also indicates a need for considering medical and surgical interventions to open the nose for the benefit of the lungs.

Conflicts of interest

None.

Sponsorships

None.

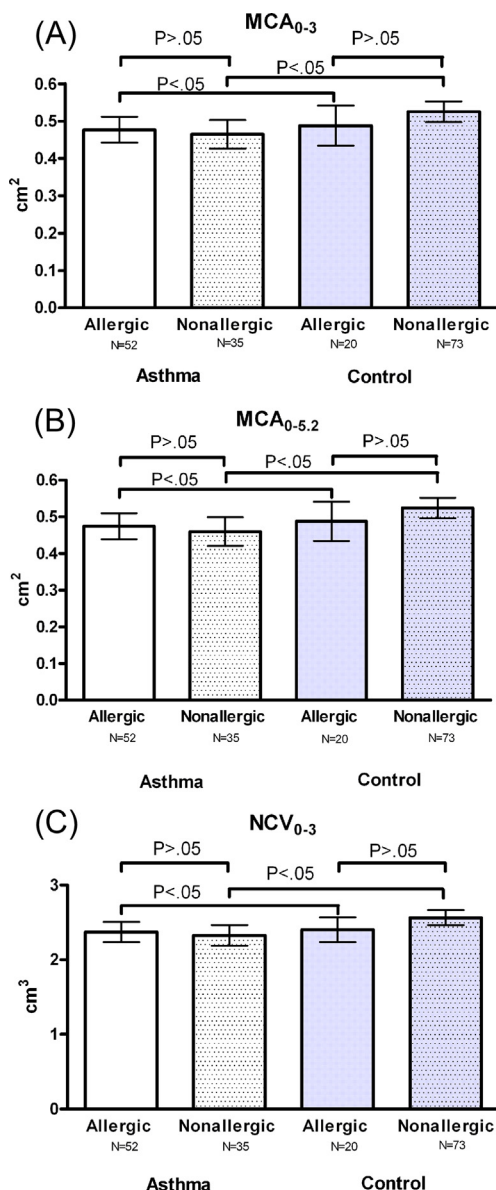


Figure 2 MCA_{0-3} (A), $MCA_{0-5.2}$ (B) and NCV_{0-3} (C) in the allergic asthmatic patients, non-allergic asthmatic patients, allergic controls and non-allergic controls. Values presented as mean, 95% CI. Abbreviations: MCA = minimum cross sectional area; NCV = nasal cavity volume; $_{0-3}$ = 0–3 cm behind the nasal orifice; $_{0-5.2}$ = 0–5.2 cm behind the nasal orifice.

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