

Nocturnal nasal obstruction is frequent and reduces sleep quality in patients with obstructive sleep apnea

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Keywords

breathing, nasal anatomy, nose, survey, apnea, acoustic measurement

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Accepted in revised form 26 September 2017; received 3 July 2017

DOI: 10.1111/jsr.12631

SUMMARY

The prevalence and consequences of nasal obstruction in untreated obstructive sleep apnea patients are not known. The study objectives were to investigate the frequency of subjective and objective nasal obstruction in untreated sleep apnea patients and the associations with sleep and quality of life. Patients in the Icelandic Sleep Apnea Cohort were subjected to a type 3 sleep study, answered questionnaires and had their nasal dimensions measured by acoustic rhinometry. In total, 810 patients participated (including 153 females), aged 54.5 ± 10.6 years [mean \pm standard deviation (SD)] with an apnea/hypopnea index $44.7 \pm 20.7 \text{ h}^{-1}$. Nocturnal nasal obstruction (greater than or equal to three times per week) was reported by 35% of the patients. These patients had smaller nasal dimensions measured by the minimum cross-sectional area within the smaller nasal valve (0.42 ± 0.17 versus $0.45 \pm 0.16 \text{ cm}^2$, $P = 0.013$), reported more daytime sleepiness (Epworth Sleepiness Scale score 12.5 ± 4.9 versus 10.8 ± 5.0 ; $P < 0.001$) and slightly lower mental quality of life than patients without nocturnal nasal obstruction. Nocturnal nasal obstruction is reported in one-third of the sleep apnea patients and they are more likely to suffer from daytime sleepiness and slightly reduced quality of life than other sleep apnea patients.

INTRODUCTION

Healthy people normally breathe through the nose during sleep, with only 0–4% of the sleeping time reported as oral breathing (Fitzpatrick *et al.*, 2003). Nasal obstruction is a problem reported by approximately 15% of the general population (Eriksson *et al.*, 2011), with decreased quality of life as consequence (Hellgren, 2007). Several structural problems may cause reduced nasal patency, including septal deviation, enlarged turbinates and nasal valve collapse. Moreover, inflammatory diseases of the nasal mucosa, such as allergic and non-allergic rhinitis, as well as chronic rhinosinusitis with and without nasal polyposis, can cause nasal obstruction (Georgalas, 2011). We have reported

recently that patients with nasal obstruction due to chronic rhinosinusitis with nasal polyps had impaired sleep quality that improved with surgery, and that the obstructive sleep apnea (OSA) risk was also decreased (Värendh *et al.*, 2017).

Obstructive sleep apnea is a common disease, affecting 25–50% of middle-aged people in the general population (Heinzer *et al.*, 2015). Using questionnaires, Hoffstein *et al.* (1992) asked patients for side effects during continuous positive airway pressure (CPAP) treatment and reported that nasal obstruction was a common issue. However, the degree of nasal symptoms before CPAP treatment was not reported, and the patients had been on CPAP for varying lengths of time. Krakow *et al.* (2016) studied non-allergic nasal obstruction retrospectively in patients referred to a sleep

investigation, but they did not specify differences in nasal obstruction between patients with and without OSA. Furthermore, they found more daytime sleepiness in patients with non-allergic nasal obstruction. No randomized controlled study has shown effect of nasal surgery on the apnea-hypopnea index (AHI) (Koutsourelakis *et al.*, 2008), but one meta-analysis showed a minor effect (Wu *et al.*, 2017). Two small meta-analyses by Ishii *et al.* (2015) and Li *et al.* (2011) concluded that nasal surgery in OSA patients with nasal obstruction leads to a decline in daytime sleepiness.

Several papers state that many OSA patients have nasal obstruction, but no well-defined, large studies have addressed the prevalence of subjective and objective nasal obstruction in these patients before initiating treatment. The pathophysiological role of the nose and the consequences of nasal obstruction for health-related quality of life in OSA are therefore not understood fully. Accordingly, the objectives of this study were to investigate the frequency of subjective and objective nasal obstruction in OSA patients while untreated, and to assess if nasal obstruction was associated with sleep-related symptoms and quality of life.

Our hypothesis was that subjective nocturnal nasal obstruction is common in OSA patients and is associated with objective narrowing of one nasal passage. Moreover, we hypothesized that nasal obstruction would influence insomnia and some other aspects of sleep quality or quality of life.

METHODS

Study design and study subjects

This is a cross-sectional study. The Icelandic Sleep Apnea Cohort (ISAC) is a project with the overall aim of studying the genetics of OSA. The project is performed in collaboration between the University of Iceland Reykjavik, Iceland and the University of Pennsylvania, USA. The major project is divided into many smaller studies, investigating different aspects of the OSA disease. Patients diagnosed with OSA who were referred to the Department of Respiratory Medicine and Sleep, Landspítali—The National University Hospital (LSH) of Iceland—for treatment with positive airway pressure (PAP) from September 2005 to December 2009 were invited to participate in the ISAC study. More than 90% of eligible and approached subjects ($n = 822$) agreed to participate and started PAP treatment following baseline assessment. Nine patients were excluded due to missing acoustic rhinometry (AR) data and one withdrew from the study (Fig. 1).

Furthermore, two patients were excluded, as they did not answer the question concerning nocturnal nasal obstruction. No other exclusion or inclusion criteria were used (Arnardottir *et al.*, 2013). The National Bioethics Committee of Iceland, the Data Protection Authority of Iceland and the Institutional Review Board of the University of Pennsylvania approved the ISAC study. All patients signed a written informed consent.

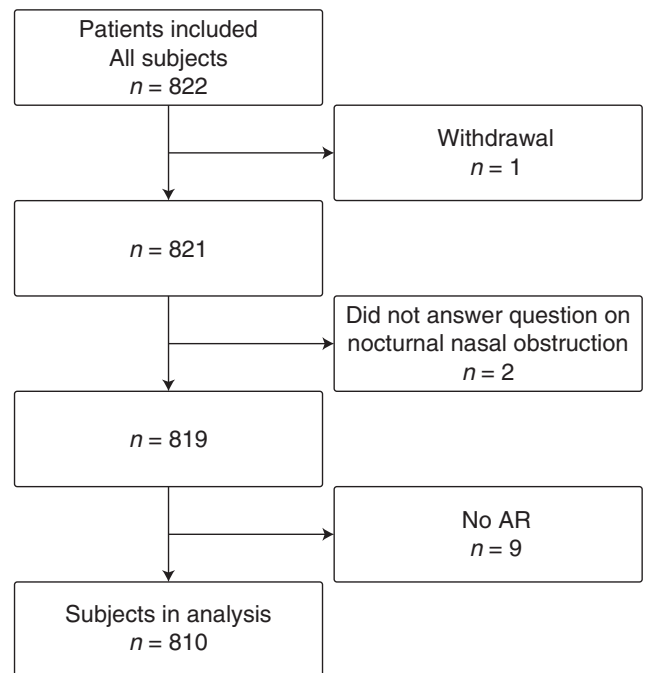


Figure 1. Outline of the patient sample.

Measurements and questionnaires

While untreated, the patients answered standardized questionnaires about their health and sleep. Nasal obstruction was evaluated with the question: 'Is your nose congested at night?'. The response categories were a frequency scale from 1 to 5: 1 = never or very seldom, 2 = less than once a week, 3 = once to twice a week, 4 = 3–5 times a week, and 5 = every night or almost every night of the week. A score of 4 or 5 was defined as nocturnal nasal obstruction. Patients completed the questionnaires the same day or, for some within the days before, were examined with Acoustic Rhinometry.

The Basic Nordic Sleep Questionnaire was used to evaluate sleep symptoms including insomnia symptoms (Partinen and Gislason, 1995). The following questions were asked: 'I have difficulties falling asleep at night' (initial insomnia), 'I wake up often during the night' (middle insomnia) and 'I wake up early and find it difficult to fall back asleep' (late insomnia). Symptoms of insomnia were considered present if reported three times per week or more often. All questions were based on the past month's experience. Nocturnal sweating was also considered present if reported three times per week or more often. Nocturnal gastroesophageal reflux was considered present if reported more than once per week (Emilsson *et al.*, 2012; Gislason *et al.*, 2002).

Daytime sleepiness was evaluated with the Epworth Sleepiness Scale (ESS), and an ESS score of ≥ 10 was considered excessive daytime sleepiness (Johns, 1991).

Health-related quality of life was examined with the Short Form Health Survey (SF-12) questionnaire (Ware *et al.*, 1996). Scores are divided into either physical or mental

health scores. Physical health is exemplified as moving a table or climbing several flights of stairs and if physical activities were limited due to compromised physical health. Concerning mental health, patients were asked if emotional issues such as feeling depressed or anxious have limited their daily activities. The scores range from 0 to 100 (score of 100 indicates the best health-related quality of life).

Patients were also asked if they were on nasal cortisone medication (yes/no).

Acoustic rhinometry

The AR technique works through an acoustic pulse sent into the nostrils. A single-impulse rhinometer (RhinoScan™ SRE2000; Rhinometrics, Assens, Denmark) was used. The method provides an anatomical description of the measurements of the nasal cavity. It compares the amplitude (representing the area) of sound waves that are reflected by the structures in the nasal cavity of an incident sound wave as a function of time (representative for the distance to the nasal cavity) (Clement and Gordts, 2005). Patients were examined sitting in an upright position.

The variables examined before nasal spray were: total minimal cross-sectional area in both nasal valves added together (TMCA, cm²), minimal cross-sectional area within the smaller nasal valve (either left or right) (MCA-min, cm²), total volume of left and right nasal cavity added together (TVOL, cm³) and the difference between MCA before and after nasal decongestive spray (MCA-diff, cm²). The decongestive spray, oxymethazoline (0.5 mg/ml) was given with two puffs in each nostril after the first AR. All AR measurements were re-evaluated on 2–6 of November 2015 by M.V. Three measurements were not of sufficient quality and were not used in calculations.

Sleep study

A type 3 sleep study was conducted with an Embletta portable monitor, an Embla 12 channel system (Embla™; Flaga Inc., Reykjavik, Iceland) or a T3 device (Nox Medical, Reykjavik, Iceland). All systems recorded the same channels. The sleep study included nasal airflow, oxygen desaturation, pulse, chest and abdominal movements by respiratory inductive plethysmography as well as body position and activity by accelerometer.

All sleep studies were re-read by a centralized scoring laboratory at the University of Pennsylvania using the Somnologica Studio (Embla™) software and were used for the analysis. More than 4 h of a scorable oxygen saturation (SaO₂) signal was needed for a sleep study to be scored. The AHI was defined as the mean number of apnea and hypopnea per hour of recording (upright time excluded). A hypopnea was classified as $\geq 30\%$ decrease in the flow with $\geq 4\%$ oxygen desaturation or $\geq 50\%$ decrease in flow for ≥ 10 s, with a sudden increase in flow at the end of the event. The oxygen desaturation index (ODI) was defined as the

number of transient drops in oxygen saturation $\geq 4\%$ per hour of recording. OSA severity was defined as: severe OSA (AHI ≥ 30), moderate OSA (AHI 15–29.9) and mild OSA (AHI 5–14.9). See previous publications for further details (Arnarottir *et al.*, 2012).

Nasal surgery

Information on prior nasal surgery was derived from patient files, including septoplasty, turbinectomy and endoscopic surgery, sometimes with polypectomy.

Statistical analysis

Nominal data were presented as frequencies and percentages without decimals. In comparisons between nominal data in independent groups, the chi-squared test was used. Fisher's exact test was used when the expected values were insufficient for a chi-squared test. Ordinal and quantitative data were presented by mean and standard deviation (\pm SD). Independent group differences were calculated with the Mann–Whitney *U*-test for two groups and Kruskal–Wallis test for more than a two-group comparison. *Post-hoc* tests were calculated with the Mann–Whitney *U*-test between two groups when the Kruskal–Wallis test showed a significance of <0.05 for more than two-group comparisons. Multiple Logistic regression analyses were calculated with the Enter method; SPSS version 22.0 was used in all analyses. A two-sided *P*-value of <0.05 was considered significant in all calculations. All *P*-values, significant or not, are presented in the comparisons.

RESULTS

Study sample

The characteristics of the patients are shown in Table 1 (153 females and 657 males). The mean \pm SD BMI was 33.5 ± 5.7 kg m². A large proportion of the patients (57%) was diagnosed with hypertension; 21% were current smokers and 27% were former smokers. Hypertension was more frequent in females ($P < 0.05$). Daytime sleepiness was common, and the overall mean score for ESS was 11.7 ± 5.0 (mean \pm SD). Also, the SF-12 survey demonstrated a low mental and physical health-related quality of life. A larger proportion of the women reported nocturnal sweating, nocturnal gastric reflux and insomnia (both initial, middle and late) ($P < 0.05$).

A majority of the patients (73%) had severe OSA; 23% had moderate OSA and 3% had mild OSA.

Prevalence of subjective and objective nasal obstruction in OSA

Overall, 65% reported nasal obstruction during the night once per week or more often and 35% greater than or equal to

Table 1 Women had smaller nasal dimensions, more insomnia and a lower quality of life

Baseline characteristics, nasal dimensions and sleep quality (n = 810)

	All n = 810	Female n (%) 153 (19)	Male n (%) 657 (81)	P-value for sex comparison
Age (years)	54.5 ± 10.6	58.6 ± 9.0	53.6 ± 10.8	<0.001
Current smoker	21%	19%	22%	0.58
Body mass index (kg m ²)	33.5 ± 5.7	34.1 ± 6.3	33.3 ± 5.5	0.19
Weight (kg)	104.3 ± 19.2	93.0 ± 17.2	106.9 ± 18.7	<0.001
Hypertension	57%	67%	55%	0.03
Diabetes	11%	12%	11%	0.70
Coronary heart disease including coronary heart occlusion, heart failure or/and stroke	18%	10%	20%	0.006
Apnea-hypopnea index	44.8 ± 20.7	42.2 ± 20.0	45.4 ± 20.8	0.058
Oxygen desaturation index (4%)	35.5 ± 20.3	32.6 ± 20.5	36.2 ± 20.2	0.008
Nocturnal nasal obstruction ≥3 × week	35%	37%	35%	0.68
TMCA (cm ²)	1.06 ± 0.31	0.94 ± 0.28	1.08 ± 0.31	<0.001
MCA-min (cm ²)	0.43 ± 0.16	0.40 ± 0.15	0.44 ± 0.17	0.02
TVOL (cm ³)	4.10 ± 0.81	3.48 ± 0.65	4.25 ± 0.77	<0.001
Diff TMCA (cm ²)	0.19 ± 0.21	0.16 ± 0.20	0.20 ± 0.22	0.02
Diff MCA-min (cm ²)	0.10 ± 0.12	0.08 ± 0.11	0.11 ± 0.12	0.03
Diff TVOL (cm ³)	0.21 ± 0.34	0.22 ± 0.31	0.21 ± 0.35	0.30
Nocturnal gastroesophageal reflux ≥ 1 × week	14%	18%	13%	0.006
Initial insomnia, ≥3 × per week	16%	27%	13%	<0.001
Middle insomnia, ≥3 × per week	58%	62%	57%	<0.001
Late insomnia, ≥3 × per week	28%	33%	27%	<0.001
Nocturnal sweating ≥3 × per week	31%	33%	31%	<0.001
Daytime sleepiness (ESS)	11.7 ± 5.0	11.2 ± 5.2	11.8 ± 5.0	0.23
Mental quality of life (SF-12)	48.3 ± 10.9	46.8 ± 11.1	48.6 ± 10.8	0.048
Physical quality of life (SF-12)	40.2 ± 10.9	35.5 ± 10.9	41.3 ± 10.6	<0.001

ESS, Epworth sleepiness scale; Diff MCA-min, difference between MCA-min before and after nasal decongestant spray; Diff TMCA, difference between TMCA before and after nasal decongestant spray; Diff TVOL, difference between before and after nasal decongestant spray; MCA-min, minimal cross-sectional area within the smallest nostril of either left or right before decongestant spray; TMCA, total minimal cross-section area in the nose, left and right nostril combined before nasal decongestant spray; TVOL, total volume of left and right nasal volume combined before nasal decongestant spray

SF-12: The 12-Item Short Form Health Survey (SF-12), a smaller version of the SF-36 version 2 Health Survey.

MCA: minimal cross-sectional area within one nasal valve, before nasal decongestant spray; TVOL: total volume of left and right nasal volume combined before nasal decongestant spray.

Significance shown in bold type.

Numbers given as mean ± standard deviation if not specified, and P-values when comparing mean values calculated with Mann-Whitney U-test.

The chi-squared test was used for comparisons between nominal data in independent groups (here shown as %).

three times per week. No significant differences were seen in OSA severity, as measured by the AHI, between the three groups ($P = 0.57$) (Table 2).

Nasal cavity dimensions assessed by AR showed mean values of TMCA 1.06 ± 0.31 , MCA-min 0.43 ± 0.16 and TVOL 4.10 ± 0.81 . TMCA and TVOL were significantly smaller in female patients than in males ($P < 0.05$) but no sex differences were found in subjective nocturnal nasal obstruction; see Table 1.

Sleep-related symptom and nocturnal nasal obstruction

We divided the patients into three groups, depending on their subjective nocturnal nasal obstruction symptoms (Table 2). Women and men were distributed equally between the three

groups ($P = 0.45$). There was a difference between the groups in MCA-min, assessed by AR, with the smallest mean value of 0.42 ± 0.17 cm² in the nocturnal nasal obstruction group compared to 0.45 ± 0.16 cm² in the group without any nocturnal nasal obstruction (*post-hoc* analysis between 'never nasal obstruction' and 'greater than or equal to three times per week', $P = 0.013$) (Table 2).

Late insomnia was reported by a larger proportion of the patients with nocturnal nasal obstruction more than three times per week compared to the group without (*post-hoc*: $P = 0.013$) (Fig. 2, P -value = 0.005 is calculated between all three groups); 65% of patients with nocturnal nasal obstruction greater than or equal to three times per week have middle insomnia. Patients with nocturnal nasal obstruction also had more daytime sleepiness compared to patients

Table 2 Patients with frequent nocturnal nasal obstruction were slightly more likely to have one smaller nasal valve; no other significant differences were found between the groups

Nocturnal nasal obstruction (n = 810)				
	Never n = 285	1–2 × per week n = 240	≥3 × per week n = 285	P-value
Age (years)	55.4 ± 10.4	53.7 ± 10.3	54.1 ± 11.0	0.16
Current smoker	21%	27%	20%	0.85
Body mass index (kg m ²)	33.7 ± 5.8	33.1 ± 5.6	33.6 ± 5.6	0.30
Apnea–hypopnea index	43.5 ± 10.0	45.8 ± 20.5	45.2 ± 21.5	0.57
Oxygen desaturation index	34.3 ± 19.8	36.1 ± 20.0	36.3 ± 20.9	0.54
TMCA (cm ²)	1.11 ± 0.30	1.07 ± 0.30	1.03 ± 0.32	0.19
MCA-min (cm ²)	0.45 ± 0.16	0.44 ± 0.17	0.42 ± 0.17	0.04*
TVOL (cm ³)	4.10 ± 0.83	4.13 ± 0.78	4.08 ± 0.81	0.78
Diff TMCA (cm ²)	0.17 ± 0.21	0.21 ± 0.19	0.20 ± 0.23	0.11

Diff MCA-min: difference between MCA-min before and after nasal decongestant spray; Diff TMCA: difference between TMCA before and after nasal decongestant spray

Diff TVOL: difference between before and after nasal decongestant spray; CA-min: minimal cross-sectional area within the smallest nostril of either left or right before decongestant spray

TMCA: total minimal cross-section area in the nose, left and right nostril combined before nasal de-obstruction spray; TVOL: total volume of left and right nasal volume combined before nasal decongestant spray. Significance shown in bold type.

Numbers given as mean ± standard deviation if not specified.

Independent group differences were calculated with Kruskal–Wallis test for >2-group comparison of mean values.

The chi-squared test was used for comparisons between nominal data in independent groups (here shown as %).

*P-value for *post-hoc* test: 0.013 comparing the groups ‘Never’ and ‘≥ 3 × per week’.

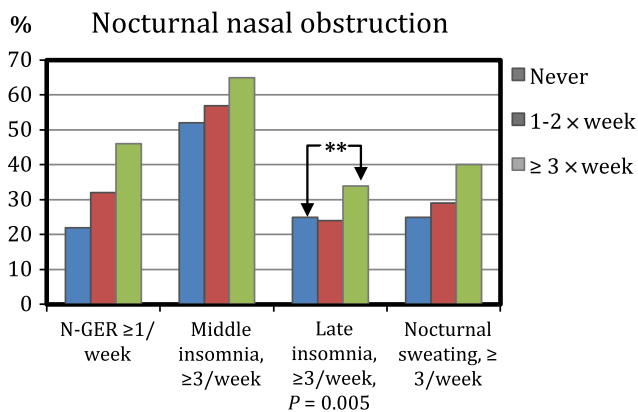


Figure 2. Patients with nocturnal nasal obstruction are more likely to have late insomnia and 65% of patients with nocturnal nasal obstruction greater than or equal to three times per week have middle insomnia. **Significance between the groups of patients without and with nocturnal nasal obstruction greater than or equal to three times per week. N-GER, nocturnal gastroesophageal reflux.

without nocturnal nasal obstruction (ESS: 12.5 ± 4.9 versus 10.8 ± 5.0, *post-hoc* comparison, $P < 0.001$) (Fig. 3). Mental quality of life was reported lower in the group with nocturnal nasal obstruction compared to those without obstruction (46.4 ± 11.4 versus 49.8 ± 10.5, $P < 0.001$) (Fig. 3).

A multiple regression analysis was performed to predict subjective nocturnal nasal obstruction. The differences found in subjective nocturnal nasal obstruction remained significant after adjusting for sex, BMI, nocturnal gastroesophageal reflux and smoking.

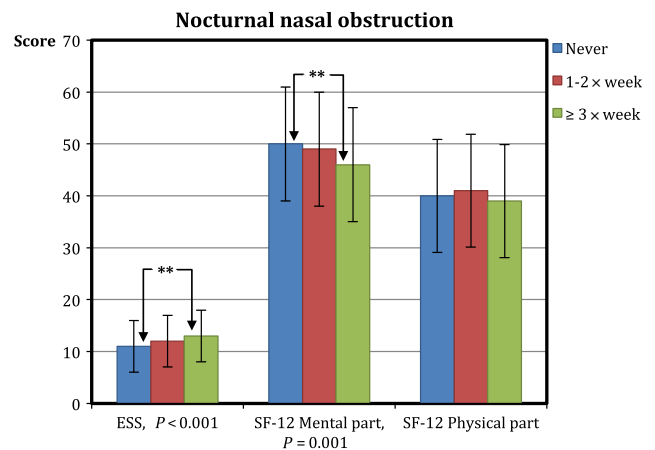


Figure 3. Patients with more nocturnal nasal obstruction have more daytime sleepiness and lower scores on quality of life, mental section. The figure describes nocturnal nasal obstruction and daytime sleepiness (ESS, Epworth Sleepiness Scale) and quality of life measured by SF-12. **Significant difference between the groups of patients without and with nocturnal nasal obstruction greater than or equal to three times per week.

Nasal surgery

A total of 86 patients had nasal surgery prior to PAP treatment and prior to being included in the study. Some patients underwent more than one kind of surgery and 18 patients underwent nasal surgery on two occasions. The different surgeries were: septal deviation surgery (61), turbinoplasty (37) and endoscopic sinus surgery and

Table 3 Former nasal surgery had no impact on AHI or nasal dimensions; a larger proportion of patients with previous nasal surgery were reporting nocturnal nasal obstruction

Former nasal surgery			
	Nasal surgery n (%)	No nasal surgery n (%)	P-value
	86 (11)	724 (89)	
Apnea–hypopnea index	40.7 ± 16.2	45.3 ± 21.1	0.12
TMCA (cm ²)	1.05 ± 0.30	1.05 ± 0.31	0.99
MCA-min (cm ²)	0.43 ± 0.16	0.43 ± 0.17	0.95
TVOL (cm ³)	4.06 ± 0.75	4.11 ± 0.81	0.84
Nocturnal nose obstruction	47%	34%	0.02

MCA-min: minimal cross-sectional area within the smallest nostril of either left or right before decongestant spray; TMCA: total minimal cross-section area in the nose, left and right nostril combined before nasal decongestant spray; TVOL: total volume of left and right nasal volume combined before nasal decongestant spray.

Significance shown in bold type.

Numbers given as mean ± standard deviation if not specified, and P-values when comparing mean values were calculated with the Mann–Whitney U-test.

The chi-squared test was used comparisons between nominal data in independent groups (here shown as %).

polypectomy (11). As a group, these patients reported significantly more frequent nasal obstruction compared to the others, despite surgery (47% versus 34%, respectively, $P = 0.02$), but no differences were found in OSA severity or measured nasal dimensions (Table 3).

Medication

Concerning medication with a possible impact on nasal obstruction, the following results were found: 37 patients used nasal steroids, 14 patients systemic steroids and six patients oral antihistamines. A total of 55 patients had one or more of these medications. However, there were no differences between the users of these drugs and non-users in terms of AHI ($P = 0.8$), TMCA ($P = 0.34$), MCA-min ($P = 0.77$) or TVOL ($P = 0.66$).

DISCUSSION

The present study demonstrates that the prevalence of reported nocturnal nasal obstruction was 35% in untreated OSA patients. Patients with nocturnal nasal obstruction were more likely to have one small nasal valve area (MCA-min). Moreover, OSA patients with nasal obstruction reported symptoms of late insomnia and daytime sleepiness slightly more often, and generally had a lower mental quality of life compared to OSA patients without nasal obstruction.

Prevalence of nocturnal nasal obstruction

The present study revealed a nocturnal nasal obstruction prevalence of almost 65% once per week or more often and 35% greater than or equal to three times in treatment-naive OSA patients. To our knowledge, the prevalence of nasal obstruction in OSA has not been described previously. A previous retrospective study reported a prevalence of non-allergic nasal obstruction of 45% in unselected sleepy patients (Krakow *et al.*, 2016). The Wisconsin Sleep Cohort reported nasal obstruction to be a risk factor for apneas, hypopneas and habitual snoring (Young *et al.*, 1997). However, they did not report a prevalence of nasal obstruction in patients with OSA.

Acoustic rhinometry

The minimal cross-section area within the smallest nasal valve of either left or right side, MCA-min, was the only parameter that was found to differ between OSA patients with and without nasal obstruction. In contrast to our results, Vidigal *et al.* (2013) used AR to study the nasal geometry in a small sample of OSA patients and a control group. They found more nasal symptoms in OSA patients compared to controls, but no difference in AR values. However, they did not investigate the smallest nasal valve compared to subjective obstruction.

There are at least two elements of nasal obstruction. The first is the structural part consisting of skeletal bone and cartilage and the second is the swollen mucosa causing congestion. The latter varies with the nasal cycle, the normal ‘corporeo-nasal’ reflex, and possibly a separate airflow cycle within each nasal valve (Kahana-Zweig *et al.*, 2016). These normal events could explain the influence of MCA-min on subjective nasal obstruction in the current study. If one side of the nose is obstructed structurally, subjective nasal obstruction will increase if subjects lie on their other side; the more open (lower) half of the nose that becomes congested, the more resistant (upper) half of the nose will not be patent (Pevernagie *et al.*, 2005).

OSA severity between the groups

No differences were observed in OSA severity between the patients with and without nocturnal nasal obstruction. No other large study has, to our knowledge, investigated the relation between AHI and nocturnal nasal obstruction. There are conflicting results concerning OSA severity and impact of nasal surgery. Two previously mentioned meta-analyses by Ishii *et al.* (2015) and Li *et al.* (2011) included small, and only randomized and controlled, studies. These studies showed no improvement on OSA severity with nasal surgery. One small meta-analysis of Wu *et al.* (2017) showed an improvement of OSA severity with surgery.

Insomnia

Late insomnia was reported more often by patients with nocturnal obstruction compared to OSA patients without nasal obstruction ($P = 0.01$) despite similar OSA severity. This finding is in line with a previous study that reported more insomnia problems in patients with undifferentiated sleep problems and nasal obstruction than in patients without these problems. However, it was a retrospective questionnaire study, and the patients were not diagnosed with OSA (Krakow *et al.*, 2016). It is possible that nocturnal nasal obstruction has an influence on late insomnia in OSA patients.

Daytime sleepiness

Daytime sleepiness was found to be more slightly more pronounced in OSA patients with nocturnal nasal obstruction compared to patients without obstruction ($P < 0.001$). With a mean value of 12.5 ± 4.9 , the sleepiness will most probably have an impact upon everyday life. Our results are therefore in agreement with previous studies showing that nasal obstruction has an impact upon daytime sleepiness (Ishii *et al.*, 2015; Li *et al.*, 2011; Värendh *et al.*, 2017).

Quality of life

Mental quality of life in patients with nasal obstruction was found to be slightly lower than in other OSA patients ($P < 0.001$) and lower compared to normal reference values for healthy adults (Hilberg, 2002). This matter has not, to our knowledge, been studied previously. A possible explanation for the decreased quality of life is that patients are influenced by their nasal obstruction, which is associated with more insomnia complaints and daytime sleepiness. Nocturnal nasal obstruction might increase the problems of insomnia and daytime sleepiness, which influences quality of life.

Medication

Using oral antihistamines, nasal or systemic corticosteroids did not have an impact upon nasal dimensions.

Strengths and limitations of the study

A major strength of this study is the large, well-defined clinical cohort of OSA patients in ISAC and that the nose is examined both subjectively and objectively.

Acoustic rhinometry is a valid technique provided that the limitations are understood (Arnardottir *et al.*, 2016; Clement and Gordts, 2005). The method describes anatomical structures, but does not give extensive information about nasal function. AR is conducted in an upright position during the daytime and therefore it is difficult to draw conclusions about nasal dimensions during sleep. However, an anatomical description of OSA patients prior to treatment is lacking in the literature, and is of interest and importance.

Sleep was recorded with a type 3 sleep study without electroencephalography (EEG), and therefore it was not possible to study arousals. However, a type 3 sleep study is clinically acceptable for the diagnosis OSA (Berry *et al.*, 2015; Mols *et al.*, 2009). A limitation to the objective evaluation of insomnia in this study is that polysomnography was not used.

The nasal questions used were not validated and additional validated questionnaires, such as the Sino-Nasal Outcome Test (SNOT-22), would probably have provided a better evaluation of the patients' symptoms. Questionnaires have limitations, but subjective symptoms of patients are extremely valuable and important. It is difficult to obtain objective measurements in some issues in real-life circumstances, and the patient's complaint indicates what is affecting her/his quality of life.

A control group of healthy individuals would have been of major interest, but to gather such a large group of non-sleep-apnea patients of comparable age, sex and weight remains a future task.

Clinical implications

The findings in this study show that it is of great importance to increase the awareness of clinicians of the high incidence of nasal obstruction in OSA patients and how much it influences their daily life.

CONCLUSION

Nocturnal nasal obstruction was found in more than one-third of the OSA patients. Subjects with nocturnal nasal obstruction had, on average, one nasal valve with a smaller minimum cross-section area. Furthermore, measures of late insomnia, daytime sleepiness and mental quality of life were slightly worse compared to patients without nasal obstruction.

ACKNOWLEDGEMENTS

We would like to thank Sigrun Gudmundsdottir and Lovisa Gudmundsdottir for data collection and Eyjolfur Sigurdsson for statistical preparations. A special thank you to Professor Robin L. Anderson, Peter MacCallum Cancer Centre and the University of Melbourne for English proofreading and a valuable review of the manuscript. The authors are also thankful to Allan I. Pack, Greg Maislin, Bethany Staley, Brendan Keenan and the other staff at the Centre for Sleep and Circadian Neurobiology at the University of Pennsylvania who helped to analyse the sleep studies and other data of the cohort. NIH supported this project, grant number: R01HL072067.

AUTHOR CONTRIBUTIONS

MV took part in designing the calculations, in evaluating the results, performed statistical calculations and drafted the

paper. MA contributed to designing the calculations, took part in evaluating the results and reviewed the paper. EB contributed to designing the calculations, took part in evaluating the results and reviewed the manuscript. HH-S contributed to designing the calculations, took part in evaluating the results and reviewed the manuscript. AJ contributed to statistical analysis design and performed statistical calculations and analysis. ESA designed the study, contributed to designing the calculations, took part in evaluating the results and reviewed the manuscript. TG designed the study, contributed to designing the calculations, took part in evaluating the results and reviewed the manuscript. SJ designed the study, participated in data collection, contributed to designing the calculations and took part in evaluating the results. All authors participated in all revisions of the paper with co-authors.

CONFLICT OF INTERESTS

MV, MA, EB, AJ, TG and SJ: no conflicts of interest. HH-S received payments for lectures from the NOX, TAKEDA and RESmed companies outside the submitted work. ESA is part-time consultant for Nox Medical, Reykjavik, Iceland unrelated to this paper, outside the submitted work.

REFERENCES

- Arnardottir, E. S., Maislin, G., Schwab, R. J. *et al.* The interaction of obstructive sleep apnea and obesity on the inflammatory markers C-reactive protein and interleukin-6: the Icelandic Sleep Apnea Cohort. *Sleep*, 2012, 35: 921–932.
- Arnardottir, E. S., Janson, C., Björnsdóttir, E. *et al.* Nocturnal sweating – a common symptom of obstructive sleep apnoea: the Icelandic sleep apnoea cohort. *BMJ Open*, 2013, 3: e002795.
- Arnardottir, E. S., Verbraecken, J., Gonçalves, M. *et al.* Variability in recording and scoring of respiratory events during sleep in Europe: a need for uniform standards. *J. Sleep Res.*, 2016, 25: 144–157.
- Berry, R. B., Gamaldo, C. E., Harding, S. M. *et al.* AASM Scoring Manual Version 2.2 updates: new chapters for scoring infant sleep staging and home sleep apnea testing. *J. Clin. Sleep Med.*, 2015, 11: 1253–1254.
- Clement, P. A. and Gordts, F. Consensus report on acoustic rhinometry and rhinomanometry. *Rhinology*, 2005, 43: 169–179.
- Emilsson, O. I., Janson, C., Benediktsdóttir, B., Júlíusson, S. and Gíslason, T. Nocturnal gastroesophageal reflux, lung function and symptoms of obstructive sleep apnea: results from an epidemiological survey. *Respir. Med.*, 2012, 106: 459–466.
- Eriksson, J., Ekerljung, L., Pullerits, T. *et al.* Prevalence of chronic nasal symptoms in West Sweden: risk factors and relation to self-reported allergic rhinitis and lower respiratory symptoms. *Int. Arch. Allergy Immunol.*, 2011, 154: 155–163.
- Fitzpatrick, M., Driver, H., Chatha, N., Voduc, N. and Girard, A. Partitioning of inhaled ventilation between the nasal and oral routes during sleep in normal subjects. *J. Appl. Physiol. (1985)*, 2003, 94: 883–890.
- Georgalas, C. The role of the nose in snoring and obstructive sleep apnoea: an update. *Eur. Arch. Otorhinolaryngol.*, 2011, 268: 1365–1373.
- Gíslason, T., Janson, C., Vermeire, P. *et al.* Respiratory symptoms and nocturnal gastroesophageal reflux: a population-based study of young adults in three European countries. *Chest*, 2002, 121: 158–163.
- Heinzer, R., Vat, S., Marques-Vidal, P. *et al.* Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir. Med.*, 2015, 3: 310–318.
- Hellgren, J. Quality of life in nonallergic rhinitis. *Clin. Allergy Immunol.*, 2007, 19: 383–387.
- Hilberg, O. Objective measurement of nasal airway dimensions using acoustic rhinometry: methodological and clinical aspects. *Allergy*, 2002, 57(Suppl. 70): 5–39.
- Hoffstein, V., Viner, S., Mateika, S. and Conway, J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. *Am. Rev. Respir. Dis.*, 1992, 145: 841–845.
- Ishii, L., Roxbury, C., Godoy, A., Ishman, S. and Ishii, M. Does nasal surgery improve OSA in patients with nasal obstruction and OSA? A meta-analysis. *Otolaryngol. Head Neck Surg.*, 2015, 153: 326–333.
- Johns, M. W. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, 1991, 14: 540–545.
- Kahana-Zweig, R., Geva-Sagiv, M., Weissbrod, A. and Secundo, L., Soroker, N. and Sobel, N. Measuring and characterizing the human nasal cycle. *PLoS ONE*, 2016, 11: e0162918.
- Koutsourelakis, I., Georgouloupoulos, G., Perraki, E., Vagiakis, E., Roussos, C. and Zakyntinos, S. G. Randomised trial of nasal surgery for fixed nasal obstruction in obstructive sleep apnoea. *Eur. Respir. J.*, 2008, 31: 110–117.
- Krakow, B., Foley-Shea, M., Ulibarri, V. A., McIver, N. D. and Honsinger, R. Prevalence of potential nonallergic rhinitis at a community-based sleep medical center. *Sleep Breath*, 2016, 20: 987–993.
- Li, H. Y., Wang, P. C., Chen, Y. P., Lee, L. A., Fang, T. J. and Lin, H. C. Critical appraisal and meta-analysis of nasal surgery for obstructive sleep apnea. *Am. J. Rhinol. Allergy.*, 2011, 25: 45–49.
- Mols, M., Pelle, A. B. and Kupper, N. Normative data of the SF-12 health survey with validation using postmyocardial infarction patients in the Dutch population. *Qual. Life Res.*, 2009, 18: 403–414.
- Partinen, M. and Gíslason, T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J. Sleep Res.*, 1995, 4: 150–155.
- Pevernagie, D. A., De Meyer, M. M. and Claeys, S. Sleep, breathing and the nose. *Sleep Med. Rev.*, 2005, 9: 437–451.
- Värendh, M., Johannisson, A., Hrubros-Strøm, H. and Andersson, M. Sleep quality improves with endoscopic sinus surgery in patients with chronic rhinosinusitis and nasal polyposis. *Rhinology*, 2017, 55: 45–52.
- Vidigal, T. A., Haddad, F. L. M., Gregorio, L. C., Poyares, D., Tufik, S. and Bittencourt, L. R. A. Subjective, anatomical, and functional nasal evaluation of patients with obstructive sleep apnea syndrome. *Sleep Breath.*, 2013, 17: 427–433.
- Ware, J., Kosinski, M. and Keller, S. D. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med. Care*, 1996, 34: 220–233.
- Wu, J., Zhao, G., Li, Y. *et al.* Apnea-hypopnea index decreased significantly after nasal surgery for obstructive sleep apnea: a meta-analysis. *Medicine (Baltimore)*, 2017, 96: e6008.
- Young, T., Finn, L. and Kim, H. Nasal obstruction as a risk factor for sleep-disordered breathing. The University of Wisconsin Sleep and Respiratory Research Group. *J. Allergy Clin. Immunol.*, 1997, 99: S757–S762.