DIAGNOSIS OF SLEEP-RELATED BREATHING DISORDERS: ESOPHAGEAL PRESSURE MONITORING, NASAL RESISTANCE AND POSTURAL CEPHALOMETRY

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Contents

ABSTRACT

Aims: The purpose of this study was to evaluate the usefulness and compliance of esophageal monitoring in combination with limited polygraphic recording (LPG) in snoring patients. The frequency of findings in the two-step sleep recording was assessed with special consideration of non-apneic sleep-related breathing disorders (SRBD). The study evaluated postural and decongestive changes in nasal measurements and the relationship of nasal patency and SRBD in snoring patients. Cephalometric measurements in upright and supine position were compared and the possible effects of mandibular position and nasal resistance on pharyngeal dimensions were evaluated. We used multiple stepwise regression analysis to find out which anthropometric, rhinomanometric and cephalometric variables best explained the variance in the apnea-hypopnea index (AHI).

Materials and methods: The study populations consisted of snoring patients referred to an otorhinolaryngology clinic for evaluation of snoring and/or obstructive sleep apnea (OSA). In consecutive snorers, LPG, including measurement of oxygen saturation, respiratory and leg movements, airflow, body position and snoring sound, was combined with esophageal pressure (Pes) monitoring. Patients with increased Pes variation combined with periodic breathing pattern and with normal oxygen desaturation index (ODI4) were further investigated with polysomnography (PSG). Sleepiness was assessed using the multiple sleep latency test (MSLT). Nasal influences of the transnasal catheter were measured using rhinomanometry (RMM). In the second patient sample, snorers scheduled for nasal surgery were examined using rhinomanometry (RMM), acoustic rhinometry (AR) and cephalometric analysis, each performed in upright and supine positions. All participants in this sample underwent PSG.

Results: OSA was found in at least 40% of the patients. UAR was found in five patients, but only one of these patients had clearly pathological MSLT. Fifteen percent of the patients had periodic leg movements during sleep (PLM), but they were not sleepy. Increased Pes variation was significantly related with diagnosis of OSA in the sleep studies. Increased Pes variation combined with increased ODI4 while the patient was in supine position predicted SRBD in this material. Total nasal resistance (TNR) was not significantly increased with a transnasal catheter used overnight compared with a control measurement without nasal manipulation. Patient compliance of Pes monitoring combined with an overnight sleep study was 87%.

Postural or decongestive changes in nasal measurements were not increased in snoring patients when compared with nonsnoring subjects. Patients with

OSA (AHI>10) showed increased postural changes in RMM when compared with snorers without OSA, but not when compared with non-snoring subjects. In the overall patient group nasal volumes in AR measured in supine position correlated inversely with AHI and ODI4. In the non-obese patients (BMI<30kg/m^2) TNR in RMM measured in a supine position correlated positively with both sleep parameters. The change in TNR on lying down correlated with AHI and ODI4 in the non-obese group. No significant correlations were found between nasal measurements performed in a seated position and sleep parameters. The change of body position from upright to supine with relaxation of the mandible was associated with changes in soft tissue structures and hyoid position, and decrease in pharyngeal airway. The change of mandibular position on lying down correlated with a decrease in airway space at the velopharyngeal and tonguebase levels. Nasal resistance correlated positively with retrolingual airspace measured in upright and supine positions. Nasal resistance after mucosal decongestion (TNRdec) and change in mandibular position (deltaANB) were found to be independent predictors of AHI in the non-obese patients. In the multiple stepwise regression analysis the non-obese patients and several skeletal subgroups gained high predictive power of AHI.

Conclusions: An UAR finding with excessive sleepiness was rare in this material. The transnasal catheter does not appear to increase TNR in patients without major structural abnormalities in the nasal passages. Compliance of Pes monitoring is good. Postural congestive changes were important in explaining the relationship of nasal obstruction and OSA, but their causes will need further investigation. Nasal resistance appears to augment airway collapse in the non-obese patients with less severe OSA, a finding supporting early treatment of nasal obstruction in snorers. Our findings suggest that mandibular position effects pharyngeal airway patency during wakefulness. Whether a relaxed mandibular position really can approximate to sleep-related changes in the pharyngeal airway will have to be confirmed. Studies in large patient samples are needed to show whether supine cephalometric analysis and skeletal subgroups are tools to improve prediction of AHI in the different treatment modalities of SRBD.

ABBREVIATIONS

AASM	American Academy of Sleep Medicine
AHI	apnea-hypopnea index
AI	apnea index
AR	acoustic rhinometry
ASDA	American Sleep Disorders Association
BMI	body mass index
BNSQ	Basic Nordic Sleep Questionnaire
CI	confidence interval
CPAP	continuous positive airway pressure
CT	computed tomography
CVD	cardiovascular disease
EEG	electroencephalogram
EMG	electromyogram
EOG	electro-oculogram
ESS	Epworth sleepiness scale
ICSD	International Classification of Sleep Disorders
IRR	increased respiratory resistance
LPG	limited polygraphic recording
MR	magnetic resonance
MSLT	multiple sleep latency test
MWT	maintenance of wakefulness test
NREM	nonrapid eye movement
ODI4	number of oxygen desaturations >4% per hour
OSA(S)	obstructive sleep apnea (syndrome)
P_{CO_2}	partial carbon dioxide pressure
Pes	esophageal pressure
PLM	periodic limb movements
PSG	polysomnography

PVDF	polyvinylidenefluoride mattress
RDI	respiratory distress index
REM	rapid eye movements
RERA	respiratory effort-related arousal
RMM	rhinomanometry
STM	Sosiaali- ja terveysministeriö (Ministry of Social Affairs and Health, Finland)
TNR	total nasal resistance
TNRdec	total nasal resistance after decongestion of nasal mucosa
TNRsu	total nasal resistance in supine position
TST	total sleep time
UAR(S)	upper airway resistance (syndrome)
UNR	unilateral nasal resistance
VAS	visual analogue scale
SCSB	static charge sensitive bed
SRBD	sleep-related breathing disorder
SWS	slow wave sleep

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original articles, which are referred to in the text by their Roman numerals.

I   Virkkula P, Silvola J, Maasilta P, Malmberg H, Salmi T. Esophageal pressure monitoring in detection of sleep-disordered breathing. *Laryngoscope* 2002; 112: 1264-1270.

II Virkkula P, Silvola J, Lehtonen H, Salmi T, Malmberg H. The effect of esophageal pressure monitoring on nasal airway resistance. *Otolaryngol Head Neck Surg* 2001; 125: 261-264.

III Virkkula P, Maasilta P, Hytönen M, Salmi T, Malmberg H. Nasal obstruction and sleep-disordered breathing: the effect of supine body position on nasal measurements in snorers. *Acta Otolaryngol (Stockh)* 2003; 123; 648-654.

IV Virkkula P, Hurmerinta K, Löytönen M, Salmi T, Malmberg H, Maasilta P. Postural cephalometric analysis and nasal resistance in sleep-disordered breathing. *Laryngoscope* 2003; 113:1166-1174.

Some unpublished data have also been included. The publishers of the original articles have kindly granted their permission to reprint the papers in this thesis.

INTRODUCTION

Population-based studies have shown that at least two percent of women and four percent of men of middle age have OSA syndrome (OSAS) (Young et al 1993). During the recent decade even mild SRBD has been demonstrated to be a cause of daytime sleepiness. Diagnosing these conditions with traditional PSG is a time consuming and expensive procedure and usually PSG is not available for primary assessment of large populations of snorers. The recognition of upper airway resistance syndrome (UARS) has set further requirements for diagnosis of SRBD. To date the prevalence of this disorder in the population is unknown. Limited sleep studies are under continuous evaluation and should meet the criteria of reasonable cost and high sensitivity to screen or diagnose SRBD. Pes monitoring is a direct measurement of respiratory effort and the method recommended for assessment of upper airway resistance syndrome (UARS) (Guilleminault et al 1993, AASM 1999). Patient compliance and nasal influences of this method have not been evaluated.

Previous reports of patients with nasal packing and seasonal allergic rhinitis have shown an increase of SRBD with nasal obstruction (Zwillich et al 1981, McNicholas et al 1982, Millman et al 1996). Several studies have demonstrated impaired nasal breathing in patients with snoring (Young et al 1997a) or sleep apnea (OSA) (Lofaso et al 2000). Nasal resistance is considered to be an important determinant of total respiratory resistance (Anch et al 1982), but the poor or lacking correlation between nasal obstruction and severity of sleep apnea has been puzzling and have raised questions of the role of nasal obstruction in SRBD (Atkins et al 1994, Lofaso et al 2000). Nasal measurements have usually been performed in an upright position. Recumbency may increase nasal resistance, but to date, the role of postural changes in patients with snoring and OSA have been insufficiently evaluated.

Cephalometry has been used extensively in orthodontics and anthropology to record craniofacial form. Investigation of soft-tissue abnormalities and pharyngeal airway in patients with OSA during the last decades has usually been performed using the standardized upright cephalometric method. Collapsibility in the pharyngeal airway is greater in patients with snoring than in nonsnoring subjects even during wakefulness (Scwab et al 1993). Magnetic resonance (MR) imaging, computed tomography (CT) scanning and occasionally also cephalometric imaging is performed in the supine position, but the method has not been strictly standardized.

In the present study we wanted to evaluate the usefulness and compliance of Pes monitoring in combination with LPG in snoring patients. The frequency of findings in this limited sleep recording and PSG was assessed with special

consideration of non-apneic SRBD. The study evaluated postural and decongestive changes in nasal measurements of snoring patients and the relationship of SRBD and nasal patency measured both in upright and supine positions. Cephalometric radiographs were obtained to investigate postural changes in the pharyngeal airway and the relationship between nasal measurements, relaxed mandibular position and pharyngeal airspace. We used postural cephalometric variables, RMM and anthropometric data to find predictors of SRBD.

REVIEW OF THE LITERATURE

1 Epidemiology of sleep-related breathing disorders

Sleep leads to narrowing of the upper airways. The dynamic changes during breathing may cause vibration of the pharyngeal structures and snoring. Depending on the individual susceptibility to pharyngeal narrowing snoring, upper airway resistance (UAR) or obstructive sleep apnea may develop.

1.1 Prevalence of habitual snoring

In the follow-up studies of snoring men and women an increase of habitual snoring in mid-life is seen. However, after 65 years age a remission of snoring seems to occur (Martikainen et al 1994, Honsberg et al 1995, Lindberg et al 1998). In a cross-sectional study of employees between 30 and 60 years of age the highest prevalences were found among men between 50 and 60 years. Fifty three percent of men and 31% of women in this age group reported habitual snoring (Young et al 1993). Large population based studies have shown an increasing trend in prevalence of habitual snoring up to the age group of 60-69 years in Finland (Koskenvuo et al 1985) and up to 60-70 years in Spain (Durán et al 2001). In the Finnish study of 7511 men and women aged 40-69 years only 9% of men and 3.6 % of women reported habitual snoring, but other studies have reported higher prevalences among middle-aged populations: 44% in men and 28% in women in the USA and 28-44% and 6-19% in Finland, respectively (Koskenvuo et al 1985, Martikainen et al 1994, Young et al 1993).

1.2 Prevalence of obstructive sleep apnea

Follow-up studies of snoring patients usually show an increase of obstructive respiratory events with age (Pendlebury et al 1997, Lindberg et al 1999). Weight gain can explain a part of the progression. However, in a study of 55 patients mild to moderate OSA seemed to have a tendency to worsen in the absence of significant weight gain. Predictive factors in upper airway anatomy or clinical variables explaining the progression were not found (Pendlebury et al 1997). Preliminary results from adult population studies support the findings, that OSA is a progressive disease at least in middle age. Obesity, age and habitual snoring were associated with increased progression of OSA at the 8-year follow-up (Young et al 2002).

In cross-sectional epidemiological studies high variation of prevalences of OSA are found due to differing criteria for OSA and the population studied (Lavie et al 1983, Telakivi et al 1987, Stradling and Crosby 1991, Young et al 1993). Young et al (1993) investigated a random sample of 602 employed men and women with an age range from 30 to 60 years. In this study all habitual snorers and 25% random sample of those not reporting habitual snoring were enrolled for PSG. The prevalence of AHI 5 or higher was estimated in 9 percent for women and 24 percent for men. When symptoms of daytime hypersomnolence were taken in account, two percent of women and four percent of men met the minimal diagnostic criteria for OSA syndrome.

The prevalence of OSA increases with age being highest in middle-aged men (Young et al 1993, Bixler et al 1998). In premenopausal women the prevalence of OSA is lower, but it seems to increase substantially after menopause (Bixler et al 2001). Increased number of patients with OSA according to laboratory criteria has been found also in the elderly over 65 years of age (Ancoli-Israel et al 1991). In an epidemiological study with a wide age range from 20 to 100 years OSA syndrome was found in 3.3% of men, when the diagnosis was based on both sleep laboratory criteria of AHI≥10 and the presence of daytime symptoms. The prevalence of any type of sleep apnea, central and obstructive, in the polysomnography (PSG) increased with age, but central apnea seemed to account for the monotonic relationship with age. Additionally, the severity of any type of sleep apnea decreased with age after 65 years when controlling for body mass index (BMI) (Bixler et al 1998). More conservative laboratory criteria for the elderly have been suggested. In children below 7 years the minimum prevalence of OSA is in the range of 1 to 3% (Ali et al 1993, Gislason and Benediktsdóttir 1995).

1.3 Prevalence of upper airway resistance syndrome

Population-based studies on prevalence of UAR are lacking. In healthy postmenopausal women without symptoms suggestive of sleep apnea, partial upper airway obstruction, manifesting as an increased respiratory resistance pattern in a static-charge-sensitive bed (SCSB), was found in 17.7% of the subjects (Polo-Kantola et al 2003). In clinical studies of symptomatic patients 6% of men and 11% of women were reported to have UARS (Votteri et al 1994, Guilleminault et al 1995a). Comparison of different studies is difficult due to various methods used and lack of a consensus regarding diagnostic criteria (AASM 1999).

1.4 Risk factors for snoring and sleep apnea

Gender and age

Men have 2- to 3-fold greater risk of sleep apnea than women, but mechanisms underlying this difference are not clear. Results from a recent study suggest that increased collapsibility in the pharyngeal airway in men is based on anatomical differences (Malhotra et al 2002a). The reasons for differences in prevalence of OSA with age are poorly understood.

Obesity

In 1995, an expert committee convened by the World Health Organisation gave a recommendation for overweight with cut points of 25, 30 and 40 kg/m^2. BMI of 25 kg/m^2 is now commonly used for the upper limit of healthy weight and BMI of 30 kg/m^2 is used as a cut point for obesity (WHO 2000). Obesity has become more common during the last decades world wide and nearly 20% of men and women in Finland are now obese with BMI>30 kg/m^2 (Flegal et al 1998, Lahti-Koski et al 2001).

Obesity is a major risk factor for OSA, although OSA can be found in non-obese subjects as well. The relationship between OSA and obesity has been demonstrated in studies of weight loss. In a randomized controlled study of 15 moderately obese patients and 8 control subjects, matched for age, weight and severity of apnea, dietary weight loss of 9% decreased apneas from 55 to 29 events/hour (Smith et al 1985). In an observational study of 690 employees during a 4 year period a 10% weight gain predicted a 32% increase in AHI and 10% weight loss predicted a 26% reduction in AHI (Peppard et al 2000a). The distribution of fat seems to make difference in the risk of obesity to OSA. Neck circumference is more closely related to the severity of OSA than BMI (Stradling and Crosby 1991). Studies using tissue specimens and MR imaging have shown increased muscle mass and deposition of fat in pharyngeal tissues in patients with OSA (Stauffer et al 1989, Schwab et al 1995). More fat deposits surrounding the pharynx were found in obese patients with OSA than control subjects matched for BMI (Horner et al 1989). Even relatively non-obese subjects with OSA may have increased fat anterolateral to the pharynx when compared with control subjects with same levels of BMI and neck circumference (Mortimore et al 1998). Other signs of upper body obesity, such as larger waist-hip ratio, subscapular skin fold thickness and visceral fat accumulation have been related to OSA (Millman et al 1995, Shinohara et al 1997).

Nasal obstruction

In a study population of 1001 men 10.4% of the subjects reported that they had nasal stuffiness often. In a multiple linear regression model the history of nasal

stuffiness contributed to the snoring as a third variable after neck circumference and smoking (Stradling and Crosby 1991). In a population-based study of 4916 men and women 6% of the sample reported that they had nocturnal nasal congestion always or almost always and another 12 % had this symptom often (Young et al 2001). Nocturnal nasal congestion occurring always or almost always was found to be an independent risk factor for habitual snoring with an odds ratio of 3.0 (95% CI, 2.2-4.0). The association was not explained by snorers with sleep apnea in a subsample studied with PSG. In subjects with chronic long-term nasal congestion at night the odds of habitual snoring increased from 3.6 (95% confidence interval, CI 2.1 to 6.3) to 4.9 (95% CI 2.8 to 8.8) in a 5-year follow-up. In a former report of Young and her coworkers a subsample of 911 subjects underwent a sleep study and measurements of nasal airflow by anterior RMM in a seated position. Habitual snorers had significantly lower nasal airflow than nonsnorers. Nasal congestion seemed to be related to habitual snoring regardless of AHI (Young et al 1997a).

An association has been found between history of nasal congestion and snoring (Stradling and Crosby 1991, Young et al 2001) and between measured airflow and history of habitual snoring (Young et al 1997a), but the relationship of nasal congestion and sleep apnea has been inconsistent. Some studies have found increased nasal obstruction in patients with OSA compared to normal subjects or non-apneic snorers (Blakley and Mahowald 1987, Lenders et al 1991, Lofaso et al 2000). Most of the studies have not succeeded in finding of a linear correlation between nasal obstruction and apneic activity (Blakley and Mahowald 1987, Lenders et al 1991, Stradling and Crosby 1991, Atkins et al 1994, Young et al 1997a). Further, Miljeteig and his collegues (1992) found no significant differences in the frequency of patients with different severity of sleep apnea in the three nasal resistance groups: normal, high unilateral and high bilateral. However,in one study a low,but significant correlation was found by posterior rhinomanometry performed in the upright position between total nasal resistance and AHI both before and after nasal decongestion (Lofaso et al 2000). In a stepwise multiple regression analysis nasal resistance explained 2.3% of variation in AHI.

Smoking, alcohol and drugs

The major independent risk factors for snoring in a large population-based study of 2187 subjects were male gender, age between 40 to 64 years, obesity and current cigarette smoking. The effect of smoking was suggested to be a consequence of increased inflammation and edema in the upper airway (Bloom et al 1988). Wetter and his colleagues (1994) found an increased risk of snoring and moderate to severe OSA in current smokers compared to never smokers. The odds ratio for non-apneic snoring was 2.3 (95% CI 1.4 to 3.7) and for at least moderate OSA 4.4 (95% CI 1.5 to 13.0). Heavy smokers (≥40 ciga-

rettes per day) had the greatest risk for OSA with odds ratio of 6.7 for mild and 40.0 for severe OSA.

In a study of 5200 adults aged 65 and older the number of alcoholic drinks was positively associated with self-reported loud snoring in men (Enright et al 1996). The central nervous system mechanisms of alcohol-induced obstructive events include depression of arousal responses to airway occlusion and reduced muscle tone (Krol et al 1984, Berry et al 1992). After ingestion of 1ml of ethanol per kg of body weight the activity of genioglossus muscle in normal subjects decreased significantly, but no changes in the function of ventilatory pump muscles could be detected (Krol et al 1984). Nasal mucosal engorgement caused by vasodilation may play a part in the adverse effects of alcohol on breathing during sleep by decreasing intrapharyngeal pressure (Issa et al 1982, Robinson et al 1985). Bentzodiatzepines and narcotic analgesics are respiratory depressants requiring special consideration when nocturnally administered to patients with OSA (Sanders et al 2000).

Familial aggregation and craniofacial characteristics

Familial clustering of subjects with OSA has been recognized. In a study of 561 members of 91 families the prevalence of sleep-disordered breathing was 21% in the relatives of index OSA patients compared with 12% in the control families. The odds of SRBD increased from 1.3 in subjects with one affected relative to 2.3 in subjects with three affected members in the family. Obesity did not seem to explain the risk of SRBD related to family membership (Redline et al 1995). In another study 105 adult offsprings of 45 randomly selected patients with OSA underwent PSG. The prevalence of OSA by laboratory criteria, 47%, was much higher than in the population in general (Pillar and Lavie 1995). First-degree relatives of patients with OSA have been demonstrated to have retroposed maxillae and mandibles, shorter mandibles, longer soft palates and wider uvulas compared with age, sex, height and weight matched controls (Mathur et al 1995). A high and narrow hard palate associated with daytime symptoms of sleepiness or tiredness has been demonstrated to be more common in first-degree relatives of patients with OSA (Guilleminault et al 1995b). Ethnicity may have an impact on prevalence of OSA and differences in associations of OSA with obesity and craniofacial measures between races have been suggested (Redline et al 1997).

1.5 Outcomes of obstructive breathing

Daytime sleepiness

Both OSA and non-apneic snoring seem to be causes of daytime sleepiness. In the Sleep Heart Health Study with a sample of 1824 participants a progressive increase in the Epworth Sleepiness Scale (ESS) score with increasing AHI was found. The mean ESS score was 7.2 in subjects with the AHI less than 5 and 9.3 with an AHI of 30 or greater. An increase in sleepiness was observed also in mild OSA compared with subjects with AHI less than 5. Most of the subjects with AHI of 5 or greater did not report excessive daytime sleepiness when estimated by ESS (Gottlieb et al 1999). Although self-reported symptoms in chronic sleepiness may underestimate the prevalence of daytime sleepiness, a high variation of inter-individual susceptibility to sleepiness in SRBD seems probable (Young et al 2002). ESS score increases with increasing frequency of snoring and the relationship between snoring and sleepiness has been found at each level of AHI, suggesting that snoring is associated with sleepiness independent of AHI (Gottlieb et al 2000). Moreover, habitual snorers with AHI less than five are three times more likely to experience multiple motor vehicle accidents compared to subjects without habitual snoring (Young et al 1997b). Daytime sleepiness in OSA is considered to be a consequence of sleep fragmentation by arousals due to apneas and hypopneas. However, the frequency of arousals, did not explain variation of sleepiness by snoring frequency (Gottlieb et al 2000).

Motor vehicle and occupational accidents

Accidents related to falling asleep are estimated to comprise 16-20% of all motor vehicle accidents (Horne and Reyner 1995). Odds ratio for multiple motor vehicle accidents in men and women between 30-60 years ranged between 2.9 in habitual snorers with AHI<5 and 7.3 in subjects with AHI>15 (Young et al 1997b). Subjective assessment of sleepiness did not explain the association of accidents and OSA. Masa and his colleagues (2000) identified sleepy subjects reporting that they feared falling asleep while driving from a random population sample of 4002 drivers. When respiratory effort-related arousals (RERA) were included in the definition of OSA, subjects with automobile accidents had a significant over 8-fold risk for having a total respiratory event index ≥15. Lindberg and her colleagues (2001) studied risk for occupational accidents by questionnaires and national register data. Men reporting both snoring and excessive daytime sleepiness had a two-fold risk for occupational accidents during the following 10 years.

Cognitive function and quality of life

The severity of OSA is related to diminished psychomotor efficiency, suggesting that SRBD may impair fine visuomotor control and sustained attention and concentration (Kim et al 1997). Findings of an association between deficits in memory and SRBD have not been found in population-based studies possibly due to methodological reasons (Jennum and Sjol 1994, Kim et al 1997). In a study of 100 self-reported snorers OSA was associated with factors reflecting memory and signal discrimination (Adams et al 2001). Even mild OSA is related to lower general health status. The effect of OSA on quality of life is comparable with that of other chronic disorders of moderate severity (Finn et al 1998).

Hypertension and cardiovascular morbidity

OSA has been found in up to 38% of patients with hypertension (Worsnop et al 1998). Several large epidemiological studies have found an independent association between OSA and hypertension after controlling the most important known confounding variables (Nieto et al 2000, Bixler et al 2000, Peppard et al 2000b, Durán et al 2001). In 6132 men and women participating in the Sleep Heart Health Study the odds ratios increased from 1.1 (95% CI 0.9-1.3) in subjects with AHI 1.5 to 4.9 up to 1.4 (95% CI 1.0-1.8) in subjects with AHI 30 or over (Nieto et al 2000). In the study of Durán et al (2001) even patients with the AHI less than 5 had an increased risk for hypertension. In the study by Bixler and his coworkers (2000) an odds ratio of 1.6 (95% CI 1.1-2.20) was found in snorers with the AHI of zero compared to subjects without snoring or SRBD (Bixler et al 2000). The odds of developing hypertension in 4 years' follow-up were increased by 42% in subjects with an AHI 0.1 to 4.9 at baseline on comparison with AHI of zero. The risk for presence of hypertension was 2-fold in subjects with an AHI 5 to 14.9 and nearly 3-fold in those with an AHI 15 or more (Peppard et al 2000b).

Significant cross-sectional association between cardiovascular disease (CVD) and OSA was shown among 6424 participants of the Sleep Heart Health Study. All subjects underwent an unattended polysomnography at home. The risk of having at least one manifestation of CVD, heart failure, stroke or coronary disease, was 42% higher in subjects with AHI of 11 or higher than participants with AHI 1.3 or less after adjustment for multiple confounding factors (95% CI 1.1 to 1.8). The risk of CVD seemed to increase, when AHI rose from zero to 10 and reached a plateau thereafter (Shahar et al 2001). However, in large prospective epidemiological studies the association between snoring and CVD has been inconsistent.

2 Upper airway anatomy and respiratory physiology

2.1 The nose

The upper airway consists of nose, pharynx, larynx and extrathoracic trachea (Kuna and Remmers 2000). The nasal airway is divided into two separate passages by nasal septum. These nasal passages are further partially divided into meatuses mainly by inferior and middle turbinates. The nasal septum is composed of membranous, cartilaginous and bony septum. The nasal valve is a slit shaped opening of about 30-40mm^2, being the smallest passage for total respiratory airflow in the respiratory tract in Caucacians. It is formed by the junction of the upper lateral cartilages, the nasal septum, and the inferior turbinate. In contrast to the main nasal passage the vestibular and valvular portion of the nasal passages is collapsible. Alar muscles dilate the nares during labored breathing, such as during exercise. However, collapse will follow increased pressure gradient between ambient and respired air (Proctor 1982, Baroody 1999). The activity of alae nasi muscle, dilator of the nasal airway, decreases at sleep onset in healthy men (Wheatley et al 1993a).

Vestibular skin transforms into squamous and transitional epithelial lining in the valvular region, and further posteriorly most of the nasal cavity is covered by ciliated columnar secretory epithelium (Proctor 1982). Nasal turbinates increase the mucosal surface of the nasal cavity and change the airflow from laminar to turbulent facilitating humidification, filtration and temperature regulation of inspired air. Alternating filling of venous sinuses in the nasal mucosa between nasal passages is referred to in the literature as the "nasal cycle" (Eccles 1999). The mechanism controlling this phenomenon is not yet fully understood. The degree of congestion seems to be determined by the balance of nasal blood flow filling the capacitance vessels and the sympathetic tone regulating smooth muscle contraction in the walls of venous sinuses (Eccles et al 1996). Although the nasal cycle has been reported to be present in up to 70-80% of subjects (Hasegawa and Kern 1978, Lenz et al 1985), the more strictly defined alternating pattern of the nasal cycle seems to be present in only 20-25% of subjects (Flanagan and Eccles 1997). Spontaneous changes in nasal airflow are found also during sleep (Hudgel and Robertson 1984). Nasal breathing seems to be the preferable route of breathing during wakefulness and sleep (Olsen and Kern 1990).

Increase in arterial CO_2 leads to vasoconstriction, whereas hyperventilation has been reported to increase nasal resistance (Dallimore and Eccles 1977). Physical exercise causes vasoconstriction of the nasal mucosa probably due to increase in sympathetic tone (Dallimore and Eccles 1977). Pain and fear will increase circulating adrenaline and decrease nasal resistance. Tactile stimuli and warming of skin of face or body can also modulate nasal resistance (Eccles 1982).

Factors affecting nasal resistance include temperature, humidity, posture and nasal cycle. Smokers seem to have increased nasal obstruction when compared to nonsmokers (Numminen 2003). Allergens are potent modulators of nasal resistance and mechanical stimulation may cause sneezing, which is usually related to increase nasal congestion and secretion (Eccles 1982). Unilateral mechanical stimulation has been shown to increase blood flow and secretion in both nasal passages of anesthetized dogs, a mechanism referred in the literature as nasonasal reflex (Lacroix and Potter 1999).

Physical and chemical stimuli to the nasal mucosa may cause reflex responses ranging from sneezing accompanied by dilation of nasal blood vessels and watery nasal secretion to bradycardia and apnea. The respiratory and cardiovascular reflexes are mediated by branches of the trigeminal nerve (Eccles 1982). Some evidence suggests that trigeminal afferent impulses from the nose may modulate respiratory movements and pattern (Ramos 1960). The existence of nasopulmonary reflex causing increase of pulmonary resistance and hypoxemia is controversial (Mirza and Lanza 1999).

2.2 Control of breathing during sleep

Normal sleep

Sleep is divided into nonrapid eye movement (NREM stages I-IV) and rapid eye movement (REM) sleep. The four stages of NREM sleep present a progressively slower electroencephalographic (EEG) activity and characteristic transients, called spindles and K complexes, during stages 2, 3 and 4. REM sleep is characterized with bursts of rapid eye movements, muscle atonia and shallow, irregular breathing. REM is further divided into tonic and phasic REM according to eye movements. In the adult sleep is initiated with NREM sleep, which then alternates with REM sleep in cycles of about 90 minutes described graphically as a hypnogram (Rechtschaffen and Kales 1968). Longer REM periods occur mainly during the last part of nocturnal sleep.

Effects of sleep on respiratory control

On sleep initiation the higher ventilatory stimulus related to wake state and the volitional influences in ventilation subside. An automatic or metabolic control system, consisting of chemoreceptors, vagal intrapulmonary receptors and brainstem mechanisms, principally influences regulation of ventilation during sleep (White 2000). Ventilatory responses to hypoxia and hypercapnia are reduced during NREM sleep and further depressed during REM sleep. Decrease in muscle tone during sleep increases respiratory resistance and inability to compensate these changes probably contributes to the reduced responses (Wiegand et al 1988). Partial carbon dioxide pressure (P_{CO_2}) is an important regula-

tor of respiratory rythmicity during sleep (Skatrud and Dempsey 1983). Periodic variation of breathing amplitude, i.e. periodic breathing pattern and central apnea is seen at high altitude during sleep (Berssenbrugge et al 1983). Hypoxia leading to hyperventilation and hypocapnia has been suggested as the mechanism of this respiratory instability. Periodic breathing is commonly found in normal subjects at sleep onset, during unsteady NREM sleep, when even central apneas may occur (Krieger 2000a). The level of P_{CO_2} is higher during sleep and P_{CO_2} levels of awake state may not be adequate to stimulate breathing at this time (White 2000). The delay in the feedback mechanisms of the chemoreceptor response may lead to hypoxia and hypercapnia and to a subsequent arousal. This will increase the duration of unsteady NREM sleep (Krieger 2000a). Increased ventilatory responses to hypercapnia may predispose to periodicity in breathing (Chapman et al 1988). During stable NREM sleep ventilation is regular, but frequent transitions between sleep stages may disrupt this rhythm (White 2000).

During REM sleep the pattern of breathing is dependent of REM sleep processes, but chemical regulation of ventilation seems to be present as well (White et al 1985a).

2.3 Effect of sleep on pharyngeal muscle function

Changes in the function of respiratory pump and upper airway muscles contribute to the increase in upper airway resistance and decrease in ventilation during sleep in healthy subjects (Wiegand et al 1990, Hudgel and Hendricks 1988, Krieger 2000a). During NREM sleep the phasic electromyographic (EMG) activity of genioglossus and geniohyoid muscles is well maintained (Wiegand et al 1990, Basner et al 1991, Tangel et at 1992). Tonic activity of upper airway dilators decreases during NREM sleep, especially in muscles without inspiratory phasic activity (Wiegand et al 1990, Tangel et al 1991, Tangel et al 1992). Decrease in lung volume during NREM sleep can further increase respiratory resistance (Hoffstein et al 1984).

Local factors, such as negative pressure, airflow resistance, airway deformation, or muscle stretch, seem to affect the function of pharyngeal dilators. Findings in a recent study indicate that negative pressure stimulus independently modulates genioglossal activity during wakefulness both within breaths and between breaths (Malhotra et al 2002b). Local anesthesia of the upper airway can reduce or abolish the activation of pharyngeal dilators by negative pressure stimulus, suggesting that superficial receptors mediate this response. So far, the nature and location of these receptors is obscure, but also nasal receptors mediating this response have been suggested by results of selective local anesthesia (Horner et al 1991). During NREM sleep the response to negative pressure seems to be reduced or lost (Wheatley et al 1993b).

23

During REM sleep the muscular atonia is maximal (Sauerland et al 1981). During phasic REM sleep the peak inspiratory activity of genioglossus and alae nasi muscles are decreased when compared to tonic REM sleep (Wiegand et al 1991). At this sleep stage the activity of intercostal muscles is decreased, whereas activity of diaphragm is increased and unsynchronized respiratory thoracoabdominal movements are seen in healthy subjects (Krieger 2000a).

2.4   Mechanical factors affecting upper airway patency

The change from upright to supine position decreases the pharyngeal cross-sectional area in most normal subjects during wakefulness (Fouke and Strohl 1987). During sleep gravity has been shown to play an important role in the generation of apneas, hypopneas and snoring even in healthy non-obese subjects (Elliott et al 2001).

Reduced functional residual capacity and inability of the lungs to dilate and distract the upper airway can increase collapsibility in the pharynx (Hoffstein et al 1984, Van de Graaf 1988). Neck extension increases pharyngeal patency primarily by increasing airway length (Safar et al 1959, Morikawa et al 1961, Thut et al 1993).

Sleep leads to opening of the jaw in normal subjects and even more so in patients with OSA (Hiyama et al 2000, Hollowell and Suratt 1991). Jaw opening can cause narrowing of hypopharyngeal airway (Safar et al 1959, Morikawa et al 1961, Kuna and Remmers 2000). Jaw opening varies during the respiratory cycle, in occurence of apneas and in different sleep stages (Hollowell and Suratt 1991, Miyamoto et al 1998). Increased opening of jaws in OSA patients compared with normal subjects has been postulated to be caused by progressive traction of submental muscles trying to move the hyoid bone forward in order to maintain airway patency. This enables breathing through the mouth (Hollowell and Suratt 1991). Surface adhesive forces help to maintain the position of the soft palate and tongue, if mouth is closed. Opening the mouth will allow the soft palate and tongue to move dorsally both by freeing these mucosal attachments and by dorsal rotation of the mandible with its muscular insertions (Kuna and Remmers 2000). Opening of the mouth has been demonstrated to increase upper airway collapsibility in normal sleeping subjects (Meurice et al 1996).

3 Definitions

3.1 Primary snoring and habitual snoring

The International Classification of Sleep Disorders manual defines primary snoring as loud upper airway breathing sounds in sleep, without apnea or hypoventilation (International Classification of Sleep Disorders, ICSD 1997).

Habitual, loud and disruptive snoring has been associated with sleep-disordered breathing. Habitual snoring may be defined as snoring occurring "every night or almost every night", or during "several nights per week to every night" (Partinen et al 1995, Young et al 2001).

3.2 Obstructive apnea

An apnea is defined as cessation of airflow greater than 10 seconds in duration (ICSD 1997). During obstructive apneas respiratory movements are seen. Mixed apneas are usually classified as obstructive apneas. They begin with a central apneic component and end with obstruction and arousal.

3.3 Obstructive hypopnea

In 1988 a study of Gould and his colleagues showed, that obstructive hypopneas are clinically important and may lead to similar sleep fragmentation as apneas (Gould et al 1988). Hypopneas are detected as decrease of oronasal airflow and/or of respiratory movements. The degree of airflow reduction in hypopneas varies in different studies and a requirement of desaturation or arousal may be accompanied (Redline and Strohl 1998). The ICSD (1997) defines a hypopnea as an episode of shallow breathing (airflow reduced by at least 50%) during sleep, lasting 10 seconds or longer, usually associated with a fall in oxygen saturation. In 1997 a task force of the American Academy of Sleep Medicine gathered to give recommendations for definition and measurement methods of sleep-related breathing disorders in order to facilitate comparability of study reports. The task force did not consider it necessary to distinguish hypopneas from apneas in clinical practice. An obstructive apnea/hypopnea event was defined as a clear decrease in amplitude (>50%) of a measure of breathing or clear reduction of breathing not reaching this criteria, but associated with either an oxygen desaturation of 3% or an arousal. The event should last 10 seconds or longer (AASM 1999).

3.4 Central apnea

A central apnea (or hypopnea) is characterized by cessation (or reduction) of ventilatory effort and a subsequent absence or reduction of airflow lasting at least 10 seconds (AASM 1999, White 2000). Typically no obstruction of airways is present.

3.5 Arousals

EEG arousals are abrupt increases of EEG frequency lasting at least 3 seconds (ASDA 1992). Respiratory effort related arousal events (RERA) occur during a sequence of breaths with increasing respiratory effort leading to an arousal (AASM 1999). Autonomic or subcortical arousals are not visible in EEG, but can be detected as activation of the autonomic system, e.g. transient increase in arterial blood pressure or heart rate (Martin et al 1997a).

3.6 Periodic limb movements during sleep

PLMs lasting 2-4 seconds occur periodically with a frequency of one in every 20-40 seconds. The prevalence of PLM disorder assessed with a questionnaire using minimal diagnostic criteria proposed by ICSD has been estimated as 3.9% being more common in women (Ohayon and Roth 2002). It has been associated with daytime sleepiness or insomnia, but a recent study in a clinical sample found no relationship between rates of leg movements during sleep and sleepiness assessed by subjective or objective methods (Chervin 2001).

4 Classification of sleep-related breathing disorders

4.1 Obstructive sleep apnea syndrome (OSAS)

OSA syndrome is characterized by repetitive collapse of upper airways during sleep, causing apneas, hypopneas and increased respiratory efforts leading to arousals from sleep and daytime symptoms. Patients usually complain of excessive daytime sleepiness, impaired cognition, mood disorders, insomnia or decreased libido (Barvaux et al 2000).

Diagnostic criteria for OSA syndrome have been defined in the ICSD. In addition to findings in PSG, the diagnostic criteria of the syndrome in adults include a complaint of excessive daytime sleepiness or insomnia, frequent episodes of obstructive breathing during sleep and associated symptoms (loud

snoring, morning headaches, dry mouth upon awakening) (ICSD 1997). The latest criteria give recommendations for research purposes and have taken into account apneas, hypopneas and respiratory effort related arousals (RERAs). OSA is defined as the total number of obstructive respiratory events five or more per hour (AASM 1999).

Severity criteria for sleep related-obstructive breathing events recommended by AASM are as follows: five to 15 events per hour (mild OSA), 15 to 30 events per hour (moderate OSA), greater than 30 events per hour (severe OSA) (AASM 1999). The Finnish national program of obstructive sleep apnea recommends these same cut points to be used for the number of apneas and hypopneas per hour in clinical practice (STM 2002).

4.2 Upper airway resistance syndrome (UARS)

Partial airway obstruction without apneas was described in symptomatic children two decades ago (Guilleminault et al 1982). In 1987 Alihanka described the pattern of increased respiratory resistance (IRR) using a SCSB, a sign of partial airway obstruction typically found during loud snoring (Alihanka 1987). An IRR period is displayed as a gradually increasing amplitude of respiratory movements in the low frequency channel of SCSB and strong respiratory variation in the high frequency channel of SCSB usually lasting several minutes. Since then, findings of partial airway obstruction using SCSB have been studied both in adults and children (Polo 1992, Kirjavainen 1997). In 1993 Guilleminault and his coworkers described patients with a clinical complaint of excessive sleepiness and a non-apneic sleep disorder with arousals related to increased respiratory efforts indicated by Pes and pathological MSLT (Guilleminault et al 1993). The syndrome was named upper airway resistance syndrome (UARS). Excessive daytime sleepiness was improved in these patients by nasal continuous positive airway pressure (CPAP) therapy. Unanimous criteria for syndrome definition are lacking. Whether UARS is a distinct condition from OSA is unclear. So far, the syndrome is recommended to be included under definition of OSA (AASM 1999).

5 Diagnosis

5.1 Symptoms

Snoring is the most common symptom reported in SRBD (Douglas 1993). It is usually estimated by questionnaires rating the frequency of snoring by words like "sometimes" and "always" or by rating the frequency for night per week

snoring (Koskenvuo et al 1985, Martikainen et al 1994). Questionnaires or a visual analogue scale (VAS) may be used to assess the disturbance or loudness of snoring (Herbert et al 1976, Lim et al 1999). Although a description of snoring is usually obtained from the patient in clinical practice, questionnaires for the bed partner are also available (Lim et al 1999). The agreement between self-reported loudness of snoring and report of a spouse in 720 subjects was found moderate (Cohen's kappa in men 0.39 and in women 0.52) (Wiggins et al 1990).

Daytime sleepiness and fatigue and complaints of unrefreshing or restless sleep are frequently encountered in patients with SRBD, but daytime sleepiness is not specific for SRBD (Douglas 1993, Redline and Strohl 1998). In a Finnish population sample of 1190 subjects 7% of men and 12% of women had daytime sleepiness (Martikainen et al 1992). Choking or gasping and apneas are relatively common symptoms in SRBD reflecting the breathing disturbance during sleep. Reported apneas have high specificity for SRBD, whereas snoring is a relatively sensitive predictor of SRBD. Mood effects and impairment of daily function and quality of life associated with SRBD may present as depression, irritability, difficulties in daily tasks, social relationships and sexual function (Redline and Strohl 1998).

5.2 Clinical assessment

A physical examination including obesity, upper-body obesity, neck circumference and retrognathia is of clinical value (Strollo and Rogers 1995, STM 2002). Abnormalities in pharyngeal anatomy may include long, bulky uvula, large hypertrophied palatal tonsils, large tongue and narrow pharynx. Septal deviation, polyps, or collapse of the nasal valve on inspiration can obstruct nasal breathing. Transnasal pharyngoscopy is used in the visualisation of nasopharynx, tonguebase and larynx.

The value of history and clinical examination in predicting OSA was evaluated in a study of 594 patients referred to a sleep clinic (Hoffstein and Szalai 1993). Age, sex, BMI, observed apneas and pharyngeal examination were significant predictors of OSA. Sensitivity of the examiners impression was 60% and specificity was 63%.

5.3 Assessment of daytime sleepiness

Daytime sleepiness is subjectively evaluated by questionnaires or self-rating sleepiness scales (Hoddes et al 1973, Herbert et al 1976). Basic Nordic Sleep Questionnaire (BNSQ), rating symptoms on a five-point scale, was developed to be a basis for questionnaires in the Nordic countries and is now in wide-

spread use (Partinen and Gislason 1995). ESS evaluates the subject's likelihood of falling asleep in different situations. It has been validated among patients with SRBD before and after treatment with nasal CPAP. Eight questions on a scale from 0 to 3 give the total score of 24 in maximal sleepiness. Control subjects had ESS scores <11 (Johns 1991). ESS is now widely used in clinical and epidemiological studies (Powell et al 2001, Gottlieb et al 1999, Gottlieb et al 2000, Masa et al 2000).

The multiple sleep latency test (MSLT) and Maintenance of Wakefulness Test (MWT) are objective measurements of sleepiness. Mean sleep latency is calculated from 4-5 daytime naps in a sleep laboratory PSG. It is the average time from lights out to the first epoch of sleep. Significant daytime sleepiness is defined as mean sleep latency below 5 minutes, while mean sleep latency above 10 minutes is regarded as normal (Krieger 2000b). A study investigating 100 patients with OSAS found a wide variation of mean latencies ranging from zero to 17 minutes (Guilleminault et al 1988). The state of the subject may influence results and low latencies are not necessarily a consequence of pathological sleepiness, but may also indicate a good sleeper (Johnson et al 1991). Moreover, motivational factors can alter sleep latencies (Harrison et al 1996). MWT measures the subject's ability to stay awake while sitting passively in a non-stimulating environment. Both tests are sensitive to possible sleep deprivation during previous nights. A study comparing MSLT and MWT found that the tests do not correlate well in patients complaining of excessive daytime sleepiness (Sangal et al 1992). The authors suggested that the tests measure different components of sleepiness. MWT was found useful in evaluation of treatment results. The interpretation of the test results needs to be related to the individual professional requirements. MSLT and ESS scores were not found to correlate among patients suspected of SRBD (Chervin et al 1999).

5.4 Overnight sleep studies

Sleep-disordered breathing is characterized by recurrent apneas and hypopneas associated with oxygen desaturations and sleep fragmentation. The apnea index (AI) describes the number of cessations of airflow per hour of sleep and apnea-hypopnea index (AHI) or respiratory distress index (RDI) is an indicator of both cessations and reductions of airflow. Recently, RDI has been defined to include respiratory effort-related arousals (RERAs) (AASM 1999). The number of falls of arterial oxygen saturation level more than 4% from baseline (oxygen desaturation index, ODI4) has been useful especially in limited polygraphies and computerized settings (Douglas et al 1992, Salmi et al 1989, Svanborg et al 1990).

Polysomnography (PSG)

In-laboratory PSG is the golden standard for assessing SRBD (American Thoracic Society 1989, ASDA 1994). PSG may also be performed by in-home ambulatory recording. PSG enables assessment of the duration of sleep, evaluation of quality of sleep and the role of respiratory or other events in sleep fragmentation. Sleep stages and arousals are assessed by using EEG, electro-oculograms (EOG) and electromyogram (EMG). Airflow is measured with thermocouples or thermistors detecting variation of temperature on inhalation and exhalation near the external nares and mouth, or with a pressure transducer with a cannula placed at the nares (Redline and Strohl 1998). Although pneumotachography is the most sensitive method for measurement of flow rate, the tight-fitting facemask is uncomfortable and can disrupt sleep. Thermistor signal is nonlinear when compared with the actual flow and has been found to underestimate hypopneas (Farré et al 1998). Nasal cannula/pressure sensor, which is actually a simple pneumotachograph, has been shown to have a good agreement with a pneumotachograph in detection of apneas/hypopneas (Heitman et al 2002). Respiratory effort is conventionally assessed with strain gauges, piezoelectric recorders, inductance plethysmography, SCSB, intercostal muscle EMG or by esophageal pressure monitoring (Douglas 1995, Redline and Strohl 1998). Oximetry is always included and heart rate, body position and snoring are commonly recorded. End tidal carbon dioxide is sometimes recorded. Leg movements are usually measured by EMG (ASDA 1993) or movement detectors. Video and sound recording can help to interpret the various nocturnal events (Douglas 1995).

Limited polygraphy

In limited overnight polygraphy sleep stages and arousals are typically not assessed, i.e. EEG, EMG and EOG are not included. In a study of 200 consecutive adults evaluated for symptoms suggesting OSA PSG detected 91 patients with AHI>15 defined as OSA and 11 patients with PLM disorder. AHI could be determined with sufficient accuracy by counting apneas and hyponeas per time in bed as by time in sleep (Douglas et al 1992). Use of automatic computer-based scoring has shown moderate or high sensitivity and specificity in clinical samples with suspicion of OSA when compared with PSG (Salmi et al 1989, Svanborg et al 1990, Stoohs and Guilleminault 1992). In clinical practice the results of automatic scoring will need visual quantification of the events.

Limited polygraphic recordings usually include the minimum of oximetry, heart rate and measurement of ventilation (airflow and respiratory effort or two channels for respiratory movements). Additionally, recording of body position, leg movements, electrocardiography and snoring may be combined (ASDA 1994, Mickelson 1999).

Oximetry

The use of oximetry alone as a screening tool for SRBD has been compared with PSG in several studies. Oximetry is suitable in screening of patients with moderate or severe disease, but inadequate in mild OSA or UARS (Douglas et al 1992, Yamashiro and Kryger 1995, Epstein et al 1998). Sensitivity of oximetry was found smaller in patients with BMI<30kg/m^2 compared with obese patients. The costs saved by this screening method were found minor with concomitant loss of diagnostic accuracy (Epstein et al 1998).

Movement recording

SCSB is a mattress placed under bedclothes and covers the whole area of a bed. A movement creates a potential difference between layers of the mattress (Alihanka et al 1981). It allows measurement of respiratory movements, body movements and heart-related movements (ballistocardiogram) without technical equipment attached to the patient. The method has been validated in detection of obstructive apneas (Polo et al 1988). Respiratory variation in the high frequency band showing a characteristic pattern called 'increased respiratory resistance' was found to be related to respiratory efforts and heaviest snoring (Polo et al 1992). Computer-assisted recordings measuring respiratory and body movements with SCSB combined with other methods have been developed and validated in detection of OSA by comparison with PSG (Salmi et al 1989, Svanborg et al 1990). In a study of 55 patients daytime polysomnography and a limited polygraphy consisting of SCSB, oximetry and thermistor were recorded simultaneously. There were 3 false negative cases in the automatic analysis of the limited polygraphy with criteria based on cumulative distribution of oxygen saturation. However, the compressed graphs of the polygraphy showed a periodic breathing pattern in all 22 patients with OSA (AHI>5). Additionally, periodic breathing pattern was found in 12 non-apneic snorers (Salmi et al 1989). In another study, the combined criteria of ODI4 ≥4 and periodic respiratory movements ≥18% of TIB gave sensitivity of 100% and specificity of 67%. If only SCSB findings were considered sensitivity was 100% and specificity was 62% (Svanborg et al 1990). The polyvinylidene-fluoride mattrass (PVDF) is a piezoelectric transducer developed for noninvasive recording of respiration, heart rate and body movements (Siivola 1989).

Esophageal pressure monitoring

Pes monitoring has been applied to the investigation of respiratory mechanics and pharyngoesophageal motility (Ogura et al 1965, Singh et al 1992). Esophageal manometry reflects pleural pressure variations and is a direct measure of respiratory effort (Baydur 1982). It is regarded as the reference standard for measurement of respiratory effort (AASM 1999). Pes monitoring alone has

been found to be 100% sensitive and specific in excluding OSA (AHI<15) and identifying severe OSA (AHI>40) when compared with PSG (Reda et al 1999). It has been found suitable for ambulatory use as well (Tvinnereim et al 1995, Singh et al 1992). In a study of regular heavy non-apneic snorers Stoohs and Guilleminault described a pattern of snoring interrupted by EEG arousals. These subjects typically presented a progressive increase in peak negative Pes with snoring (Stoohs and Guilleminault 1991). A study comparing in SCSB and Pes monitoring in PSG found increases of intrathoracic pressure amplitude without clear changes in the SCSB tracings during snoring periods without apneas, hypopneas or significant desaturations (Berg et al 1995). Tolerance of the recording with catheter was 93%. Pharyngoesophageal pressure monitoring with multilevel sensors is a method suggested to give additionally information about the level of obstruction during sleep (Tvinnereim and Miljeteig 1992, Demin et al 2002).

Studies on potential effects on sleep quality using a naso-esophageal catheter have found minimal changes in sleep architecture in patients with suspicion of SDBD (Chervin and Aldrich 1997). Another study did not find any statistical difference in sleep quality between PSGs with and without esophageal catheter in a sample of patients with suspicion of OSA (Skatvedt et al 1996). Increased duration of saturation below 90% during non-REM sleep was the only significant change with catheter in place. The catheter use was found to increase sleep fragmentation in a sample of ten normal subjects and ten parasomniacs (Espa et al 2002).

Other methods for detection of respiratory effort

Respiratory effort and airflow can be measured with a pressure sensor/transducer attached to a facemask or a nasal oxygen cannula. Inspiratory limitation is shown by a characteristic plateau of the inspiratory pressure curve (Hosselet et al 1998). When compared with esophageal manometry, nasal pressure analysis has been shown to identify RERAs accurately (Ayappa et al 2000). The measurement of typical patterns in the high frequency band of SCSB and end tidal carbon dioxide (Polo et al 1992, Kirjavainen 1997) and pulse transit time (Argod et al 2000) are among the methods suggested as noninvasive alternatives for assessment of respiratory effort in non-apneic snorers.

Body position

The upper airways of patients with OSA are more collapsible in the supine position than in the lateral body position during sleep (Penzel et al 2001). Body position can be monitored by attending personnel, videotaping or by a body position sensor. Body position data is needed in evaluation of representative-

ness of a study night and for comparison of repeated sleep studies (Lojander et al 1998). OSA occurring primarily in a supine position can be treated with position therapy (Cartwright 1991).

Recording of snoring

So far, there are no standards or commonly accepted techniques for objective measurement of snoring. The placement of a microphone, calibration of the equipment, signal analysis and definition of snoring varies in different studies (Hoffstein 1996a). The agreement between objective measurement snoring sound and perception of snores among listeners has been found only moderate due to the subjective interpretation of the perceived sounds as snoring (Hoffstein et al 1996b). In a population study of Busselton town 48 middle-aged men reported that they snored "never" or "hardly ever". Only 29% of them did not snore during the study night. On the other hand, fourteen percent (n=4) of 29 subjects reporting to snore "always" did not snore on the study night (Bearpark et al 1995). Recorded snoring sounds have been found to have low specificity in detection of OSA (Stoohs and Guilleminault 1992). However, combined with oximetry high sensitivity and specificity has been reported (Stoohs and Guilleminault 1992, Issa et al 1993). Computer analysis of audio-taped snoring has been shown to identify apneas, but it is less accurate in distinguishing hypopneas (Mickelsson 1999). Increased variation of esophageal pressure in UAR may be accompanied by a crescendo type increase in snoring intensity and can help to visually identify events of increased respiratory effort (Guilleminault et al 1993).

5.5 Imaging of the upper airways

Imaging modalities used in investigation the upper airway biomechanics in OSA include cephalometry, acoustic reflection, fluoroscopy, CT scanning and MR imaging. Additionally, nasopharyngoscopy can be performed during wakefulness or anesthesia induced by propophol or midazolam. So far, there is insufficient data on the benefits of awake endoscopy in selection of patients for operative care. Acoustic reflection and fluoroscopy have been used mainly in research. Fluoroscopy allows investigation of the upper airways even during sleep, but predisposes the patient to irradiation.

Cephalometry

Cephalometry is a standardized lateral radiograph of the head and neck. It has been used in anthropology and orthodontics and more recently in evaluation of skeletal and soft-tissue structures in patients with OSA and treatment with oral

appliances or craniofacial surgery. It has gained wide use in clinical practice due to its low cost and good availability. The standardized cephalometry is performed in the upright position. A natural head position is usually obtained by the fluid level technique or by means of a mirror or a light source. A cephalostat prevents rotation of the head. The exposure is performed with teeth in occlusion (Solow and Tallgren 1971, Huggare 1985). In evaluation of snoring patients exposure at end-expiration must be used to improve repeatability of soft-tissue measurements. Measurements are usually performed in the upright position (Scwab 2001).

CT and MRI

CT scanning provides accurate imaging of the pharyngeal lumen, as well as, soft-tissue and craniofacial structures. Moreover, volumetric images and reconstruction of craniofacial structures can be obtained. Dynamic imaging is possible with this method. Disadvantages include radiation exposure and costs. CT scanning may be useful in evaluation of patients undergoing maxillomandibular advancement surgery (Schwab 2001).

MR imaging obtains better resolution for adipose tissue than CT scanning and does not expose to radiation. Three-dimensional reconstruction of soft tissue structures, accurate assessment of cross-sectional area and volume, and dynamic imaging are possible. High costs and limitations in availability have restricted its use in clinical practice (Schwab 2001).

5.6 Nasal measurements

Rhinomanometry

The principles of current RMM were described by Aschan and his colleagues (Aschan et al 1958). The method is based on simultaneous recording of the transnasal pressure and airflow. It is considered to reflect primarily the narrowest section of the nasal passage, usually the valvula, where the greatest drop of resistance occurs (Pallanch et al 1992). Active RMM refers to recording during restful respiration, whereas in the passive method the pressure is measured while the subject holds his or her breath, and air is pumped through the nose at a known rate. Active method is preferred today, because it is more physiological (Clement 1984). Airflow is measured with a nozzle or a mask, and a pneumotachograph (Broms 1982a, Clement 1984). An alternative method for measurement of airflow is plethysmography (Cole 1989a). Transnasal pressure is measured with one of three methods: 1) the tube is placed at the opening of the contralateral nostril not being tested (anterior RMM), 2) the tube is inserted into the oropharynx through the mouth (posterior RMM) or 3) the tube is inserted postnasally through either nasal passage (postnasal RMM)

(Cole 1989a). The posterior method requires coaching in correct breathing technique and fails more often than anterior RMM (Kortekangas 1972). The anterior method cannot be performed in patients with septal perforation or with total unilateral obstruction of a nasal passage. None of the rhinomanometric methods are useful if the nose is totally blocked (Pallanch et al 1992).

The International Standardization Committee for Rhinomanometry agreed that active anterior rhinomanometry is the most common and physiological technique (Clement 1984). It has made recommendations about the equipment and technique in RMM. The standard measurements should be performed in a sitting position after an acclimatization period. The committee did not give instructions about measurements performed in recumbency. Resistances given at a fixed pressure of 150 Pascal or at radius 200 in a polar coordinate system, when using Broms' model, were designated as preferable options (Broms 1982b, Clement 1984). BMI did not have an effect on nasal measurements by RMM or acoustic rhinometry (AR) in a study of young healthy adults (Numminen 2003).

The use of total nasal resistance and decongestion increases the reproducibility of measurements in RMM (Broms 1982c). Despite the reciprocating high unilateral resistances during nasal cycle, total nasal resistance remains relatively constant in a healthy nose during wakefulness and sleep (Hasegawa and Kern 1978, Hudgel and Robertson 1984). Decongestion of the nasal mucosa can be accomplished by physical exercise or sympatomimetic medication. Decongested values are considered more appropriate for evaluation of skeletal stenosis (Broms 1982c, Jessen and Malm 1984), whereas the change of resistance in decongestion, so called "decongestion effect", has been used for assessment of the role of mucosal pathology (Broms 1982c, Suonpää et al 1995). Measurement of nasal resistance after decongestion has been found useful in preoperative prediction of subjective benefit in septal surgery (Jessen and Malm 1984, Sipilä 1991).

Acoustic rhinometry (AR)

The measurement technique based on acoustic reflection was introduced by Jackson and his coworkers in 1977 and in 1989 Hilberg and his colleagues described the use of ARM in evaluation of the nasal cavity geometry. The method gives an estimate of cross-sectional area as a function of distance. An acoustic pulse propagates along a wave tube and a nosepiece to the nasal passage. The sound pulse is reflected by impedance changes caused by changes in cross-sectional area along the nasal airway. The reflecting signal is gathered by a microphone, amplified and analyzed by a computer (Jackson et al 1977, Hilberg et al 1989). The Standardisation Committee on AR encourages the use of volume 0-5cm, and volume 2-5cm for mucosal changes. They also recom-

mended reporting the two smallest minimum areas and their distance from the nostrils within the first 5 cm (Hilberg and Pedersen 2000). In a recent study cross-sectional areas were found to be more susceptible to error than volume (Djupesland and Rotnes 2001). The accuracy of acoustic rhinometry was found to be reliable up to 4 cm and moderate from 4 to 7 cm when compared with computer tomography volumetry (Numminen 2003).

Advantages of AR include quick, noninvasive measurement and need of minimal co-operation by the patient. It is therefore recommended for studies of infants (Djupesland and Pedersen 2000). AR has been found to be more rapid in capturing transient mucovascular changes after challenge allowing the use of a small dose of allergen compared with RMM (Roithman et al 1997a) and a sensitive method in detecting postural and decongestive mucovascular changes (Fouke and Jackson 1992, Kase et al 1994). Information of nasal dimensions may be beneficial in planning of nasal surgery and in evaluation of results of treatment (Roithman et al 1997b).

Magnitude of error in AR measurements increases with distance beyond 5cm with some underestimation of distant areas (Jackson et al 1977). Narrowing in the nose <6mm causes underestimation of deeper areas (Buenting et al 1994, Roithmann et al 1997b). When the cross-sectional area is small and the length of the narrowest part of the passage is short, the probability of measurement error is higher (Cakmak et al 2001). Although RMM has been found particularly sensitive in detection of airway obstruction (Cole 2000), AR was found at least equally sensitive in revealing septal deviations in the anterior nasal cavity in a study of 24 anterior septal deviations in 50 patients (Szücs et al 1998). The reproducibility of measurements repeated over time by both methods has been found to be within the range of many widely accepted clinical tests (Silkoff et al 1999).

6 Pathophysiology of upper airway obstruction during sleep

According to a "balance of forces model", the pharyngeal airway patency is dependent of inward forces produced by respiratory pump muscles and outward forces induced by upper airway dilating muscles (Remmers et al 1978). Sleep leads to decrease in muscle tone and increase of upper airway resistance. Snoring is a respiratory sound generated by vibration of the soft palate, pharyngeal walls, epiglottis and tongue (Liistro et al 1991). It occurs during inspiration and expiration and can be detected during nasal, oronasal and oral breathing (Perez-Padilla et al 1993, Hoffstein 1996a). Snoring patients may present with simple snoring, partial airway obstruction or OSA.

During wakefulness patients with OSA have narrower pharyngeal airway and increased tendency to narrowing as lung volume decreases compared to controls (Bradley et al 1986). Deposition of fat around the pharynx and neck, reduced functional residual capacity and inability of the lungs to dilate and distract the upper airway are among the mechanisms considered to increase collapsibility in subjects with OSA (Mortimore et al 1998, Hoffstein et al 1984, Van de Graaf 1988).

Airway narrowing during sleep occurs usually at the level of the soft palate or the tongue-base, or at both these sites (Hudgel 1986, Hudgel and Hendricks 1988). The site of collapse was assessed by multilevel pressure monitoring in 18 grossly obese male patients (BMI 37, SD 2kg/m^2) (Shepard and Thawley 1990). During NREM sleep the velopharynx was the site of collapse in 10 patients and the remaining patients had retroglossal airway narrowing. During REM sleep the collapse seemed to progress to a more caudal segment. In a study of 45 mostly obese patients (mean BMI 31, SD 4.6 kg/m^2) studied during hypotonia induced by CPAP, the velopharynx was the site of marked pharyngeal narrowing during sleep in most patients, but multiple sites and secondary oropharyngeal or hypopharyngeal narrowing were common (Morrison et al 1993).

In a study by Isono and his coworkers (1997), mechanical properties of the pharyngeal airway of 40 patients with OSA and 17 normal subjects were studied during paralyzation under general anesthesia. Maximal velopharyngeal area in videoendoscopy was decreased both in the milder and more severe groups of OSA compared with the group of normal subjects matched for age, BMI and sex. Oropharyngeal area was decreased only in the more severe OSA with ODI >20 supporting the hypothesis of anatomy as the primary factor in the pathogenesis in OSA. The results suggested also mechanical interdependence between velopharyngeal and oropharyngeal segments (Isono et al 1997).

Patients with OSA have increased phasic and tonic genioglossal EMG activity during wakefulness, suggesting that they need a compensatory mechanism to maintain airway patency (Mezzanotte et al 1992, Fogel et al 2001). Like in normal subjects, topical receptor mechanisms seem to influence dilator muscle activity in patients with OSA during wakefulness (Fogel et al 2000), but neuromuscular reflexes seem to be reduced during sleep. Unlike in normal subjects, genioglossal muscle activity usually decreases at sleep onset in patients with OSA (Remmers et al 1978, Mezzanotte et al 1996). The state-dependent decrease of muscle activity and possibly loss of increased EMG activity, a postulated compensatory mechanism related to OSA, may lead to airway obstruction in an anatomically narrow pharyngeal airway during sleep (Isono et al 1997). Whether patients with OSA have a greater decrease in of neural pharyngeal activity during sleep is not clear, but impairment in neural pharyngeal control possibly happens secondary to oxyhemoglobin desatura-

tions in OSA (Teramoto et al 2001). Instability of respiratory control may contribute to the severity of OSA in some patients (Younes et al 2001).

Morphological abnormalities have been found in palatopharyngeus muscle showing increase with severity of obstructive breathing (Friberg et al 1998). These findings suggest that vibratory trauma in the soft palate may lead to local sensory neuropathy in OSA. Upper airway sensation was found to be reduced in non-apneic snorers and in patients with OSA, but improved partially with nasal CPAP treatment (Kimoff et al 2001). Sensory nerve injury might increase susceptibility to airway collapse by impairing local mechanisms controlling airway patency. Moreover, some evidence of inflammation associated with OSA has been reported. The total number of cells and the number of polymorphonuclear leukocytes in nasal lavage fluid was significantly higher in eight patients with OSA compared with those in six control subjects before sleep and after sleep. Increased concentrations of bradykinin and vasoactive intestinal peptide could be measured in patients with OSA in comparison to controls before sleep and the next morning. These signs of inflammation were not associated with symptoms of rhinitis (Rubinstein 1995). Further, exhaled nasal pentane and nitric oxide levels were found increased in 20 patients with moderate or severe OSA after sleep compared with presleep values (Olopade et al 1997). So far, the role of muscle dysfunction, afferent nerve injury and inflammation in the development obstructive breathing is unclear.

An apnea or hypopnea is generally terminated by an arousal leading to increased activity of dilator muscles and re-establishment of airway patency. Isocapnic hypoxia, hypercapnia and added inspiratory resistance can lead to an arousal from sleep. In patients with OSA longer apneas are found during REM sleep (Douglas 2000). Arousals may occur after increased respiratory efforts without significant hypoxemia or hypercapnia. Since similar mean peak-negative esophageal pressure levels preceding arousal responses for different stimuli have been observed, increased respiratory effort may be the actual mechanism leading eventually to an arousal. Apnea-related sleep fragmentation is currently regarded as the main cause of daytime sleepiness in OSA (Kimoff 1996). Although subcortical, autonomic arousals have been demonstrated to cause sleepiness, the relevance of this kind of sleep fragmentation as a source of daytime sleepiness remains unclear (Martin et al 1997a, Stradling et al 2000).

7 Nasal obstruction in sleep-related breathing disorders

7.1 The influence of nasal airway on breathing during sleep

About 50% of the total respiratory resistance has been estimated to originate from nasal passages (Proctor 1977). An adequate pressure difference between the atmosphere and the intrathoracic space created during nasal breathing is considered beneficial for pulmonary ventilation (Proctor 1977). Nasal resistance prolongs expiration, increases pulmonary compliance and allows time for alveolar gas exchange. Limited nasopharyngeal airflow has been postulated to increase the transpharyngeal pressure difference and lead to airway collapse (Olsen et al 1981, Olsen and Kern 1990, Shepard and Burger 1990). The area under nasal flow volume loops has been found to contribute independently to the prediction of AHI (Shepard and Burger 1990).

Nasal obstruction has been shown to affect breathing by increase of both central and obstructive apneas (Zwillich et al 1981, McNicholas 1982, Suratt et al 1986). Stimulation of the nasal mucosa with an irritant can cause repeated episodes of apnea and hypopnea during sleep (White et al 1985b). These findings seemed to suggest that receptors in the nose inhibit respiration. Existence of flow sensitive receptors in the nose affecting respiration has been suggested (Ramos 1960). Loss of stimulation of these receptors might alter the respiratory pattern. Alternatively, change of the breathing route from nasal to oral breathing during severe nasal obstruction may increase respiratory instability (White 2000).

7.2 Causes of nasal obstruction

The most common causes of nasal obstruction are various types of rhinosinusitis, polyposis and structural nasal abnormalities. Turbinate hypertrophy is a common finding in patients with chronic rhinitis and septal deviation.

The frequency of acute upper airway respiratory infections is 1-2 per year in adult population and 3-5 per year in children (Monto and Sullivan 1993, Gwaltney 1997). Chronic rhinosinusitis has been estimated as the most common chronic disease in the United States with fourteen percent of the population being afflicted (National Center for Health Statistics 1995). Seasonal allergic rhinitis is usually found in 10% of population and and perennial rhinitis is reported in 10-20% of the population (Skoner 2001). In Finland the prevalence of allergic rhinitis is estimated as 15-20% in the adult population and 20-25% in adolescents (Haahtela and Björkstén 1998). Nasal polyps are reported

in 1-2% of the population in Europe and in 4.3% of a study sample in Finland (Hosemann et al 1994, Hedman et al 1999).

Allergic sensitization has been associated with increased risk of OSA in children (McColley et al 1997). A study of 7 adult patients with seasonal allergic rhinitis showed an increase in numbers and duration of apneas during the symptomatic period of a ragweed season (McNicholas et al 1982). Patients with astma had 40% greater chance of being a habitual snorer in a large population-based study (Young at al 2001). In 50 patients diagnosed with allergic rhinitis decongestive changes at the cross-sectional area of the valve region were found to be higher in patients with OSA compared with non-apneic patients. Additionally, high decongestive changes in cross-sectional areas and in volume from 0 to 6cm were found more often in patients with OSA (Houser et al 2002). However, in a clinical sample of adult patients presenting with typical symptoms of OSA, allergic rhinitis was not found to be a risk factor for OSA (Kramer et al 2001).

Only 21% of nasal septa in a study of adult skulls were found to be straight (Gray1978). Although the finding of a deviated septum is common, only a part of deviations are related to impaired nasal breathing. In a study of 6-15 years old children a septal deviation considered to have potential clinical significance in anterior rhinoscopy was present in 9.5% of the study population. However, symptoms or nasal function were not assessed in this study (Haapaniemi et al 1995).

7.3 Symptoms in nasal obstruction

Nearly 20% of adults complain of regular nocturnal nasal congestion. Eleven percent of the subsample reported this symptom due to allergy and 9% of participants reported other causes (Young et al 2001). Symptoms of rhinitis include rhinorrhea, nasal blockage, sneezing, itching and postnasal drip. Adult patients with rhinitis may complain of nonrestorative sleep and tiredness during the day. Adult subjects with nocturnal rhinitis symtoms often or almost always were more than twice as likely to feel unrested and to have excessive daytime sleepiness habitually (Young et al 1997a). Daytime sleepiness in allergic rhinitis has been associated to arousals and sleep fragmentation due to airway obstruction, but other mechanisms not related to breathing may also exist (McNicholas et al 1982, Young et al 1997a). Artificial nasal obstruction causes both objective and subjective disturbance of sleep (Olsen et al 1990).

The symptoms of nasal obstruction are not always correlated with objective measures of nasal patency. After treatment of nasal septal deviation 22% of patients complained of persistent nasal stuffiness despite a decrease in nasal resistance (Gordon et al 1989). Physical trauma or inflammation has been sus-

pected to alter sensation of nasal patency. However, in a clinical patient sample with structural nasal pathology and symptoms of nasal obstruction, nasal resistance and subjective sensation clearly correlated (Sipilä et al 1994).

7.4 Nasal symptoms and findings in snoring and OSA

Nasal symptoms seem to be common in patients with OSA syndrome. In a prospective study of consecutive patients blocked nose (45%), dryness (74%), sneezing (53%), postnasal drip (51%) and rhinorrhea (37%) were reported (Brander et al 1999). Nasal stuffiness was equally common, complained by 46% of patients, in a retrospective study of patients with OSA before treatment with nasal CPAP (Lojander et al 1999).

In a clinical study of 431 patients undergoing PSG for suspected OSA, nasal ventilation was found to be highly limited in 14.3% of the subjects. Nasal ventilation in RMM was highly limited in 17% of patient with OSA and in 13% of patients without OSA. Eight percent of the patients with OSA and 6% of the non-OSA patients had undergone septum surgery before the study (Mayer-Brix et al 1989).

In a study of forty-five habitual snorers and 22 patients with OSA nasal measurements by AR and RMM were compared with a control group without nasal history or significant findings in rhinoscopy or snoring. Increased nasal resistance and hypertrophy of inferior turbinates was found in most of the snoring patients. Additionally, 17% of the patients had septal deviations. Only 19% of the patients complained of nasal stuffiness (Lenders et al 1991).

7.5 Effects of artificial nasal obstruction during sleep

Evidence from studies with nasal packing and nasal obstruction during seasonal allergic rhinitis indicates that acute nasal obstruction can induce SRBD (Zwillich et al 1981, McNicholas et al 1982, Millman et al 1996). An increase of apneas and arousals and loss of deep sleep was found in 10 normal men during experimentally induced nasal obstruction with an inflatable balloon cannula (Zwillich et al 1981). In the study by Millman and his collegues (1996) of healthy older children and young adults responses to nasal obstruction varied from insignificant to marked increases of respiratory distress index (RDI). Nasal packing increased the total number of apneas, hypopneas, apnea duration and sleep fragmentation. In patients with OSA nasal packing may markedly increase obstructive events and cause a decrease in minimum oxygen saturation (Wetmore et al 1988).

7.6 The effects of nasal pathology and supine body position on airway measurements

The posterior RMM method has given 9% higher total resistance values in patients without obstructive nasal pathology when compared with postnasal method in upright measurements probably due to the pharyngeal component measured by a transoral catheter (Cole 1989b). In patients with sleep apnea the change in supraglottic airway resistance on lying down in a supine position was found to be higher than in healthy subjects and was attributed to narrowing of the pharyngeal airway in OSA (Anch et al 1982). Desfonds and his coworkers (1997) reported higher increase of resistance in posterior RMM in the supine position in snoring patients compared with nonsnoring volunteers. After decongestion the resistance remained elevated in snorers. Effects of posture and decongestion were similar whether the snorer had sleep apnea or not.

Nasal resistance increases also in anterior RMM when tilting the head down (Hasegawa 1982). The postural changes can be measured within a few minutes and have been considered as vascular (Rundcrantz 1969). Nasal resistance has been found to increase slightly also after 1-2 h of sleep in healthy subjects (Wheatley et al 1993a). In dorsal recumbency the amplitude of the nasal cycle in RMM is greater than in upright measurements. On the assumption of lateral recumbency the lower nasal cavity becomes more resistive in approximately half of subjects with clinically normal noses, but this effect seems to be overcome by the alternation of congestion during the nasal cycle (Cole and Haight 1986, Hasegawa et al 1990).

Further increased positional changes in nasal resistance have been found during acute and allergic rhinitis (Rundcrantz 1969, Hasegawa 1994). Stroud and his colleagues (1999) found that smokers and patients with rhinitis have a significantly greater TNR increase when supine compared with nonsmokers or patients without rhinitis. In patients with septal pathology subjects with high postdecongestion nasal resistance had an increased decongestive effect compared with subjects with low postdecongestion nasal resistance suggesting concomitant mucosal inflammation in the group of more severe septal deformation (Suonpää et al 1994).

During the nasal cycle resistance increases in the supine position more on the side of high resistance than in the nasal passage with low resistance in normal subjects (Hasegawa 1982). Due to the increased dependency of a patent decongested side, fluctuation of total nasal resistance during the nasal cycle can be found in recumbent patients with unilateral structural obstruction (Cole 1989c). The amplitude of cyclic changes of minimal cross-sectional area in AR in patients with septal deviation has been found to be higher in the wider nasal cavity in the upright position (Sung et al 2000). However, the amplitude of unilateral nasal resistances in patients with septal deviation was higher on the

side of obstruction (Cole 1989c). Postural changes in anterior RMM have been studied in patients with moderate or severe OSA (AHI 15-68) and velopharyngeal collapse. The authors found no statistically significant differences in AHI between the 20 patients with normal positional RMM and the 16 patients with pathologic positional RMM, defined as >30% increase in resistance from baseline seated measurements (De Vito et al 2001).

7.7 Treatment of nasal obstruction in sleep-related breathing disorders

Surgical treatment aims to relieve nasal obstruction by septal surgery, reduction of turbinate volume, polypectomy or by rhinoplastic methods. This treatment has been reported to relieve snoring in up to 90% in adult patients when snoring was measured 6-9 months postoperatively with a questionnaire (Elsherif et al 1998). Friedman et al (2000) reported improvement in snoring in 34% of patients with OSA. Data on objective improvement of measured snoring sound is lacking. In treatment of SRBD in adult patients nasal surgery has only limited efficacy. Success rates range between 0 and 33% (Friedman et al 2000, Verse et al 2002). However, nasal surgery seems to improve daytime sleepiness, and decrease arousals in both apneic and nonapneic snorers (Lavie et al 1982, Series et al 1993, Verse et al 2002). Series and his colleagues (1993) matched 14 patients with moderate OSA (mean AHI 17.0) for AHI and BMI. In 6 of 7 patients with normal cephalometry (MP-H, PAS, SNA, SNB, PNS-u1) (see study IV Figures 1, 2) AHI decreased to below 10, whereas no improvement was found in the 7 patients with abnormal cephalometry. Likewise, arousals decreased significantly in patients with normal cephalometry. A similar decrease in nasal resistance measured in a supine position was observed in both groups after nasal surgery (Series et al 1993).

Nasal septal surgery with or without turbinate resection has been shown to reduce levels of nasal CPAP needed to treat severe sleep apnea (Friedman et al 2000). Results from a randomized, placebo-controlled pilot study suggest that CPAP adherence improves after radiofrequency treatment of inferior turbinates in patients with turbinate hypertrophy (Powell et al 2001).

In children adenoidectomy is the most common surgical treatment for impaired nasal breathing. Snoring and mouthbreathing can be relieved, but in OSA it has not been found to be an adequate treatment and is recommended to be combined with tonsillectomy (Nieminen et al 2000).

External and internal nasal dilators are designed to increase airway patency at the nasal valve and have been demonstrated to improve both subjective and objective nasal nasal obstruction (Roithmann et al 1998). External dilators decreased snoring loudness evaluated by the bed partner in an uncontrolled study

of subjects with mild snoring. Ease of breathing during sleep, quality of sleep and daytime sleepiness improved significantly in self-assessment (Scharf et al 1994). The quality of life of heavily snoring men was found significantly worse when compared with a population sample. The use of an external dilator improved both daytime sleepiness and quality of life (Löth et al 1999). In another study internal dilators were not found beneficial for measured snoring or apnea in snorers without evidence of nasal obstruction in clinical examination whether they had OSA or not (Hoffstein et al 1993). In 26 patients with RDI over 10 and impaired nasal breathing mean RDI decreased significantly from 31.6 to 26.3 with the use of an external dilator (Gosepath et al 1999). RDI decreased by 50% or more in 10 patients. Inferior turbinate hypertrophy, septal deviation and/or allergic rhinitis seemed to predict a positive effect. In a randomized controlled study of 12 habitual snorers with chronic rhinitis (AHI<20), the use of an external dilator decreased objectively measured snoring frequency, but had no effect on AHI or arousal index (Pevernagie et al 2000).

8   The pharyngeal airway in patients with OSA

8.1 Craniofacial and soft-tissue abnormalities in OSA

Cephalometric studies of patients with OSA have demonstrated several abnormalities, including reduced mandibular body length, presenting as micrognathia or retrognathia, inferiorly positioned hyoid bone and retroposition of maxilla (Lyberg et al 1989a, Partinen et al 1988, Pracharktam et al 1994, Lowe et al 1995). In a clinical meta-analysis mandibular body-length was demonstrated to be significantly associated with OSA (Miles et al 1996). Skeletal craniofacial abnormalities seem to be more clearly associated with OSA in non-obese patients than in obese patients (Partinen et al 1988, Tsuchiya et al 1992, Nelson et al 1997, Sakakibara et al 1999, Tangugsorn et al 2000). Additionally, soft-tissue structures have been found to be larger in patients with OSA when compared with normal subjects (Lyberg et al 1989b, Lowe et al 1995). CT and MR imaging in these patients demonstrate increases in the size of soft palate, tongue and lateral pharyngeal walls (Lowe et al 1995, Scwab et al 1995). Both tongue and soft-palate size has been found to correlate with BMI (Lowe et al 1995, Sakakibara et al 1999, Do et al 2000). However, cephalometric soft-tissue measurements between patients with OSA and BMI-matched controls differ in many respects. Patients with OSA have a larger tongue, a more caudal position of the tongue, a larger soft palate, an inferiorly positioned hyoid bone, and decreased upper airway width at several levels (Sakakibara et al 1999).

In a recent study of cephalometry and BMI the craniofacial morphology and BMI together accounted for 65% of the total variance in AHI. The most important cephalometric variable was the horizontal length of the maxilla. BMI seemed to be a more important predictor of AHI in patients with a large antero-posterior facial dimension compared to a small antero-posterior facial dimension, whereas in non-obese subjects cephalometric dimensions were predominant contributors to AHI (Dempsey et al 2002).

A study of physical findings as predictors for OSA in a clinic population found that narrowing of the airway by the lateral pharyngeal walls, tonsillar enlargment, and enlargement of the soft palate and tongue were associated with OSA. After controlling for BMI and neck circumference lateral narrowing and enlargement of the tonsils remained significant with an odds ratio of 2.0 and 2.6, respectively (Schellenberg et al 2000).

8.2 Postural imaging during wakefulness and sleep

Only a few cephalometric studies on patients with OSA have been performed in the supine position. These measurements have been less standardized. The methods vary by position of the head, use of a cephalostat and position of the lower jaw (Yildirim et al 1991, Pae et al 1994, Pracharktam et al 1994, Ono et al 1996, Miyamoto et al 1997). A decrease in airway space at the retropalatal level in the supine position has been observed in the OSA patients (Yildirim et al 1991, Pae et al 1994, Pracharktam et al 1994, Ingman et al 2003). At the level of the tonguebase, changes in airway dimensions have been less consistent. Either widening (Yildirim et al 1991) or decrease (Pae et al 1994) or no significant changes (Pracharktam et al 1994, Ingman et al 2003) of airway space at the tonguebase level in patients with OSA has been observed. EMG activity of genioglossus muscle in healthy control subjects has been found to increase over 30% after assuming a supine body position. Airway length decreased and hyoid bone has been found to move cranially only in normal subjects. Hyoid bone moved forward in the OSA group (Pae et al 1994). Tongue length has been found to decrease in OSA and in normal subjects (Pae et al 1994, Ingman et al 2003) and the tongue seems to fall back on lying down (Pae et al 1999). Using the pharyngeal airway measurements at levels of the soft palate, tip of uvula and tonguebase a stronger correlation for RDI was found in the supine position than in an upright position (Pae et al 1994).

Sleep-related changes in cephalometry have been studied only recently in healthy volunteers (Hiyama et al 2000). The jaws open significantly and the distance between mandibular symphysis and cervical vertebra decreases after sleep onset in stage 1-2 NREM sleep. A decrease in anteroposterior width of the pharyngeal airway can be observed at the retropalatal and retrolingual airway. In patients with OSA studied by dynamic MR imaging, narrowing of the

upper airway was observed at various sites during sleep (Ikeda et al 2001). The transient narrowings at the level of the soft palate observed during tidal breathing in wakefulness changed into complete obstruction during spontaneous sleep.

AIMS OF THE PRESENT STUDY

The aims of this study were:

I   To evaluate findings of snoring patients in an overnight limited polygraphic recording with Pes monitoring in an otorhinolaryngology clinic.

II   To investigate the usefulness and compliance of Pes monitoring in combination with limited polygraphic recording as a screening tool for sleep-related breathing disorders.

III   To study positional and decongestive changes in nasal measurements of snoring patients.

IV   To evaluate the relationship of sleep-related breathing disorders and nasal patency measured by anterior rhinomanometry and acoustic rhinometry in upright and supine positions.

V   To compare cephalometric measurements of upright and supine postures and to study the relationship between mandibular position, nasal resistance and pharyngeal dimensions in snorers.

VI   To find predictors of sleep-related breathing disorders in snorers using anthropometric data, rhinometric measurements and both upright and supine cephalometric analysis.

MATERIALS AND METHODS

1 Patients and control subjects

1.1 Patients

The study population consists of snoring adult patients referred to the ENT Department of Helsinki University Central Hospital because of a snoring problem and/or suspicion of sleep apnea.

A total of 150 patients were enrolled in the four study protocols and 122 of these patients constituted the study population entering further analysis. Patient characteristics are shown in Table 1.

In study I, 107 consecutive snoring patients were asked to participate in the study protocol with esophageal pressure monitoring combined to an overnight sleep recording. Six patients refused insertion of the catheter. Two patients were excluded because of nasal problems. The catheter had to be removed because of discomfort or came off in six patients before the recording started. Five patients using sedatives were excluded. Twenty-one recordings were excluded for technical reasons. In these recordings the storage of all signals in the computer did not succeed or was too short to be representative for the study purpose. In one recording, Pes variation was obscured by cardiac pulsations. Sixty-seven patients were included in the final analysis.

In study II 50 patients undergoing LPG were studied with RMM the following morning. We excluded 3 patients for failed RMM recordings and 12 patients because control measurements without nasal manipulation were not available. One patient was excluded as his seasonal allergic nasal symptoms had started between the rhinomanometry measurements, and another patient was left out because she had used antihistamines before the study night. The patients did not have major structural deformities in the nasal the passages. Recordings of 33 patients were accepted for analysis.

In studies III and IV 43 consecutive habitually snoring men from the waiting list for correction of nasal obstruction were recruited. Forty patients underwent cephalometric analysis (study IV). Recordings RMM and AR in seated and supine positions were carried out for 41 patients (study III).

Patients using sedatives and patients with alcoholism or progressing or labile disease were not included in the studies of analysis of breathing during sleep (I, III and IV).

Table 1. Patient characteristics, RMM and sleep study data of the snoring patients (studies I-IV). Unless otherwise indicated the data represent mean values, with standard deviation in parenthesis, and range.

	Study I	Study II	Study III	Study IV
N	67	33	41	40
Females/males, n	14/53	6/27	0/41	0/40
Age, years	48 (9.7) 31-72	48 (9.4) 32-69	44 (8.9) 26-62	44 (9.6) 26-62
BMI, kg/m^2	27 (4.7) 19-44	28 (5.3) 21-44	28 (3.5) 22-37	28 (3.6) 22-37
Habitual snoring, n	55		41	40
Smoking, n	20	12	20	19
ODI4 (LPG)	4.8 (9.1) 0-38			
AHI (PSG)			13.7 (15.7) 1-54	13.3 (15.7) 1-54
TNR baseline, Pa/cm^3/s	0.266[1] (0.178) 0.070-0.913	0.269 (0.139) 0.070-0.702	0.282[2] (0.195) 0.074-0.856	
TNR decongested, Pa/cm^3/s	0.201[1] (0.161) 0.063-0.861	0.189 (0.088) 0.063-0.404	0.220[2] (0.209) 0.054-0.994	0.200[2] (0.163) 0.054-0.752

[1] n=54. [2] in 5 patients measurements in RMM failed due to severe nasal obstruction. Habitual snoring: self-reported snoring every night or almost every night; BMI: body mass index; ODI4: number of oxygen desaturations >4% per hour in bed; LPG: limited polygraphic recording; AHI: apnea-hypopnea index; PSG: polysomnography; TNR: total nasal resistance.

1.2 Control subjects (study III)

Nineteen voluntary nonsnoring control subjects (14 males and 5 females) were recruited mainly from the clinic staff for study III. Mean age was 42 years (range 31-70 years).

2 Patient history and clinical assessment

In study I a sleep questionnaire based on the Basic Nordic Sleep Questionnaire (Partinen et al 1995) was used. The questionnaire includes questions concerning sleeping habits, daytime hypersomnolence, snoring, alcohol consumption etc. For scoring of daytime sleepiness we used questions about the frequency

of daytime sleepiness and irresistible tendency to fall asleep at work and during free time. Frequencies of having fallen asleep while driving and at lessons or watching television were also included in the evaluation of daytime sleepiness. The frequencies of daytime sleepiness in the different situations were assessed on a five-point scale from score 0 (never) to score 4 (every day or almost every day). In addition, we asked the patients to estimate their daytime sleepiness on visual analogue scale (VAS) from 0 (no sleepiness) to 100 (very sleepy). Scoring of the VAS scale was performed as follows: 0-40 (0), 41-55 (1), 56-70 (2), 71-85 (3), and 86-100 (4). A total score of sleepiness was counted from the questionnaire and VAS together. Each question and VAS gave a number of points ranging from 0 to 4. Thus the total score ranged from 0 to 24 (Sleepiness score). Excessive daytime sleepiness of phase II patients in study I was reassessed with ESS (Johns 1991).

In study I snoring frequency and snoring intensity were assessed by the patients themselves on a five-point scale of the sleep questionnaire. In the patients from studies III and IV history of habitual snoring given by the patient was required when requested to participate the study.

In study III nasal history and symptoms were assessed with a separate questionnaire in addition to the sleep questionnaire.

The patients underwent an ENT examination. RMM (studies I-IV), AR (study III) and cephalometric analysis (study IV) were used to evaluate nasal obstruction and craniofacial dimensions. For assessment of sleep-related breathing disorder, LPG with esophageal pressure monitoring (study I) and PSG (studies I, III, IV) were performed. MSLT was carried out in phase II of study I.

3 Nasal measurements

3.1 Active anterior rhinomanometry

RMM (NR6-2, G.M. Instruments Ltd., Glascow, Scotland, UK) was performed after a rest period in a seated position (baseline measurement). Decongestion of the nasal mucosa was carried out by 50μg of xylometazolin hydrochloride nasal spray for each nasal passage. Inspiratory values were obtained and resistance was calculated at radius 200 according to the Broms method (Broms et al 1982b). Total nasal resistance (TNR) was calculated from the unilateral recordings (unilateral nasal resistance, UNR).

In study II RMM was measured the following morning after an overnight limited sleep study with esophageal pressure monitoring. RMM was performed in a seated position with a transnasal esophageal catheter in place, immediately

after removal of the catheter and after decongestion of the nasal mucosa. The patients were allowed to blow their noses after removal of the catheter, and measurements without a catheter were then continued. In nine of 33 RMM recordings the measurer suspected leakage of air on the catheter side. Occlusion of the nostril was difficult when the catheter was in place and this might affect the measurement of the noncatheter side. Therefore, measurements of the noncatheter side immediately after catheter removal were used to count corrected combined nasal resistance values with a catheter in place. None of the patients used antihistamines, sympatomimetics or nasal corticosteroids the day before the sleep study night. Recordings of RMM performed earlier without nasal manipulation were used for comparison.

In study III RMM was performed in a seated position (baseline), after lying down for 5 minutes in a supine position (Figure 1) and again seated after decongestion of nasal mucosa. Nasal measurements were avoided during symptomatic period in seasonal allergic rhinitis. In five measurements in a seated position, in six measurements in a supine position and in five measurements after nasal decongestion nasal resistance with anterior method could not be measured due to a severely obstructed nasal passage.

In study IV TNR was measured after lying down for 5 minutes without nasal congestion and in a seated position after decongestion of the nasal mucosa.

3.2 Acoustic rhinometry (study III)

In study IV AR (A1/2 Acoustic Rhinometer, G.M. Instruments Ltd., Glascow, Scotland, UK) was performed immediately after RMM in a seated position, after lying down for 5 minutes in a supine position (Figure 2) and again seated after decongestion of nasal mucosa. Volumes at distance 0-3cm, 2-4cm and 0-5cm from the nostril were measured. Combined volumes (VOL 0-3, VOL 2-4 and VOL 0-5) were calculated from unilateral measurements.

4 Cephalometry

Lateral cephalometric radiographs were taken in both upright and supine postures. The upright cephalograms were carried out with natural head position according to the fluid level method (Solow and Tallgren 1971, Huggare 1985). The habitual sagittal head orientation obtained, and indicated by the fluid level device, was repeated in the cephalostat. The soft-tissue filter was adjusted on the profile or the pharyngeal region to improve soft-tissue imaging. The exposure was performed at the end of expiration with teeth in occlusion. Supine ra-

diography was taken awake in a relaxed posture with a constant pillow height of 5cm. An opening of the jaws was allowed to obtain natural mandibular position.

The landmarks identified from lateral cephalograms were digitized, computer registered, and linear and angular variables were calculated (X-Metrix, Smartsystem, Turku, Finland). The skeletal reference points found in Bhatia and Leighton (1993) as well as points and lines for measurement of head posture in Solow and Tallgren (1971) have been defined accordingly (see study IV Figure 1). The radiographic magnification of 10% was corrected. The error of the method was determined by using the Dahlberg formula (Dahlberg 1940) The range of error between two registrations was 0.25-1.12 mm for the linear and 0.20-1.50 degrees for the angular measurements. Cephalometric measurements of tongue, soft palate, pharyngeal dimensions and position of hyoid bone are presented in study IV Figure 2.

Figures 1 and 2. A patient undergoing measurements of anterior RMM and AR in supine position (studies III and IV).
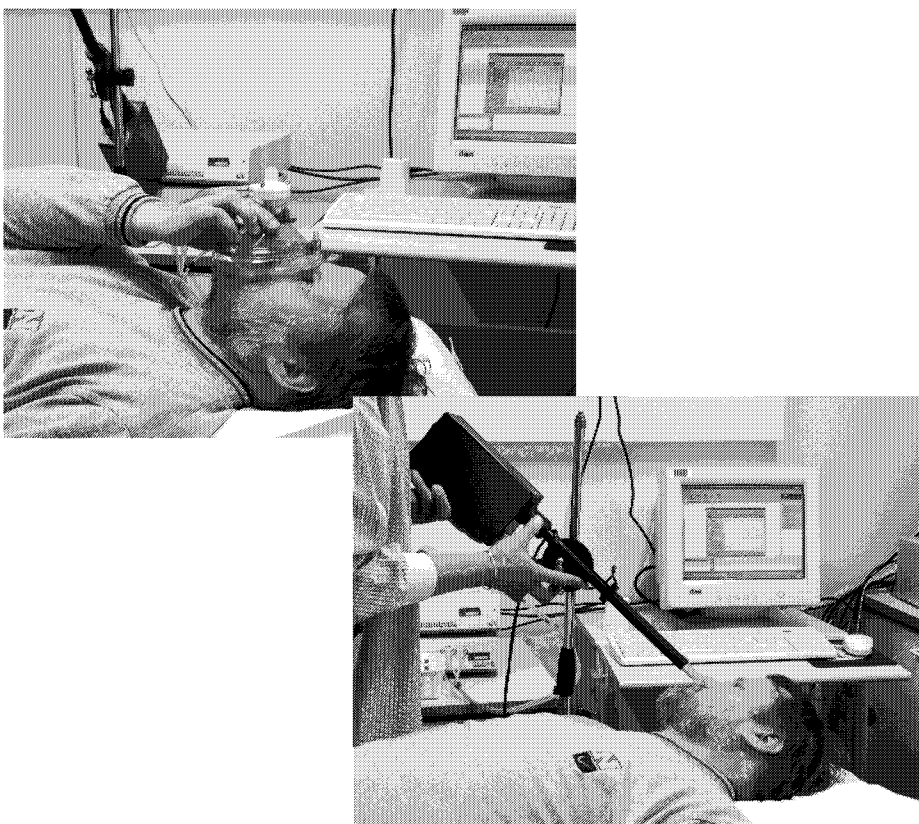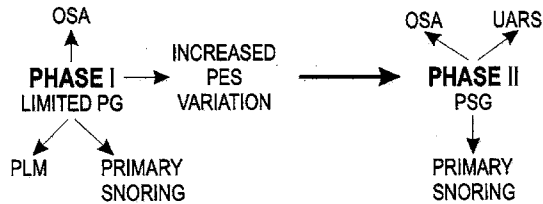
5 Overnight sleep studies

5.1 Limited polygraphic recording (LPG)

An overnight LPG with oximetry (Biox-Ohmeda, Louisville, Colorado, USA), respiratory (SCSB, Biorec, Turku, Finland, presently situated in Helsinki, Finland) and leg movement recording (PVDF sensor, Synectics Medical, Finland), and a nasal and oral thermistor and body position sensor (Finnomedical, Järvenpää, Finland) was performed on an otorhinolaryngology ward in a separate room. The raw signal of the SCSB-mattress was filtered into low (0.25-0.9 Hz) and wide (0.3-16Hz) frequency bands for measurements of respiratory and gross body movements, respectively. All variables were automatically analyzed using a computer-based program as previously described (Salmi et al 1989). Limited polygraphic recording was combined with continuous Pes monitoring (Gaeltec, Isle of Sky, Scotland, UK) and measurement of snoring with a calibrated microphone (Finnomedical, Järvenpää, Finland). Snoring sound was band-pass filtered (30-500Hz), rectified and integrated with an analog amplifier. An esophageal catheter of 2 mm diameter with a pressure transducer on the tip was placed 35 to 43 cm from the nostril (Baydur et al 1982) (Stanford standard: height x 0.228). Topical anesthesia of the nasal passage and pharynx was obtained with 10% lidocaine spray, and the catheter was inserted at least 1 to 2 hours before the patient went to bed. The processed snoring sound signal and Pes were stored on a computer disk with other signals for the analysis. Compressed graphs from computer printer including all signals were obtained for visual analysis.

Oxygen desaturations exceeding 4% (ODI4) and 2.5% (ODI2.5) from baseline were counted. The numbers of minutes of Pes variation with inspiratory negative pressure peaks higher than 10mm Hg from the baseline was counted. Snoring sound with intensity exceeding 60dB SPL (sound pressure level) at distance of 20 cm was counted as significant snoring. A recorded minute with more than 10 seconds of significant snoring was classified as a "snoring minute". All parameters were counted for the duration of time in bed. Snoring, as well as ODI4, was counted separately for the supine position. The amount of recording with periodic leg movements detected by the leg movement sensor was calculated in minutes.

The setting in study I included an overnight use of a naso-esophageal catheter during limited polygraphic recording (phase I). Patients with abnormal ODI4 (ODI4>5) in LPG were considered to have sleep apnea. Those patients with any signs of periodic breathing disturbances including periodic changes in airflow and/or respiratory movement signal, periodic snoring and especially with increased respiratory related Pes variation, but with normal ODI4 were referred for a complete PSG (phase II) (Figure 3). The mean time interval between the sleep studies was 12 months.

Figure 3. LPG was used to select the patients with respiratory related increased esophageal pressure variation as the initial finding for further studies with PSG (study I). OSA: obstructive sleep apnea; PLM: periodic leg movements; Pes: esophageal pressure; UARS: upper airway resistance syndrome; PSG: polysomnography.

```
        OSA                              OSA    UARS
         ↑         INCREASED              ↖    ↗
      PHASE I  →      PES        ────→    PHASE II
      LIMITED PG    VARIATION              PSG
        ↙  ↘                                ↓
     PLM    PRIMARY                       PRIMARY
            SNORING                       SNORING
```

5.2 Polysomnography

The overnight hospital recordings were performed using a computerized 24-channel polygraph (Alice 3, Healthdyne technologies, Marietta, GA, USA) This included a four channel EEG (C3/A2, C4/A1, O1/A2, O2/A1), electro-oculogram, and submental and leg electromyograms. Heart rate was monitored through standard leads. Airflow was detected by monitoring with a nasal and oral thermistor Thoracic and abdominal belts (Healthdyne effort sensor, Healthdyne) were used for respiratory movement detection. Pulse oximetry (BCI Oximetry 3100, BCI International, Inc, Waukesha, Wisconsin, USA) and a body position sensor (Healthdyne) were included in all recordings. A calibrated skin microphone (Healthdyne) was attached to the throat for snoring detection and the esophageal catheter was again applied.

The sleep stage was scored manually in 30-second epochs following the criteria of Rechtschaffen and Kales (1968). Respiratory and non-respiratory events were both scored visually. An apneic event was defined as absence of nasal or buccal flow for at least 10 seconds. Hypopnea was scored as the diminution of flow amplitude more than 50% and for longer than 10 seconds associated either with an arousal or an oxygen desaturation of at least 3%. The AHI was defined as the number of apneas and hypopneas per hour of sleep. An arousal was defined as an EEG frequency shift to the α range for at least 3 seconds (ASDA 1992). A respiratory event was scored when diminution of flow amplitude was observed for over 10 seconds associated with paradoxical chest and abdominal movement possibly with crescendo pattern of snoring. Respiratory effort related arousals (RERAs), preceded by an apnea, a hypopnea, or a respiratory event, were scored for patients with AHI <5 and arousals >5 per hour. PLMs were scored according to the recommendations of American Sleep Disorders Association Task Force (ASDA 1993).

6 Multiple Sleep latency test

In MSLT mean latency from lights out to the first epoch of any stage of sleep was calculated. EEG (six channels, central (C3, C4) and occipital (O1, O2) leads), submental EMG and EOG were recorded for sleep scoring (Rechtschaffen and Kales 1968). The patients had four nap opportunities with 2 hour intervals, starting usually at 8.45 a.m., but not within two hours after the usual waking time. The test was continued for 15 minutes after the first sleep epoch to discover the possible REM-onset. If sleep did not occur within 20 minutes, the test was discontinued and sleep latency was scored as 20 minutes (Thorpy 1992).

7 Statistical analysis

The data was processed with a commercial statistical package (Statistica™ v.5.1, Statsoft Inc., Tulsa, OK, USA). Differences between groups were tested using the t-test for independent samples or χ^2 frequency tables. Repeated measurements within a group were compared with the t-test for dependent samples. Pearson correlation analysis was used to evaluate the relationships between anthropometric data, nasal measurements, cephalometric measurements and sleep parameters. In study IV, multiple stepwise regression analysis was used to evaluate the contribution of antropometric, rhinometric and sleep variables in AHI. Residual autocorrelation of the model was tested by Durbin-Watson test. P-values < 0.05 were considered to indicate statistical significance.

8 Ethical aspects

The ethical committee of Department of Otorhinolaryngology of Helsinki University Central Hospital approved the study. The subjects gave their informed consent with regard to participation in the study.

RESULTS

1 Esophageal pressure monitoring in the detection of sleep-disordered breathing (studies I and II)

1.1 Patient compliance

Ninety four percent (101/107) of patients entering limited polygraphic recording accepted the esophageal catheter. An overnight catheter use was accomplished in 87% (93/107) of patients.

1.2 Limited polygraphic recording with esophageal pressure monitoring (phase I)

Characteristics and LPG data of the 67 patients are presented for the overall patient sample in Table 1. Corresponding data according to diagnosis in LPG are shown Table 2. OSA (ODI4>5) was diagnosed in 14 (21%) patients with LPG. There were no Pes changes and there was no periodic pattern of breathing movements, airflow or snoring in recordings of 24 (36%) patients.

Six patients had more than 15 periodic leg movements per hour, but they were not sleepy according to the sleepiness score. Forty-one patients (61%) had increased Pes variation. Two patients with PLM had Pes variations, but they were excluded from further analysis. Thus, 27 patients without OSA or PLM had pathologic variation of Pes with some periodic variation of other respiratory measurements.

The recordings of OSA patients showed increased Pes variation especially during apneas and this finding was significantly related to OSA diagnosis in phase I.

1.3 Polysomnography (phase II)

The twenty-seven patients with ODI4 less than 5 and increased variation of Pes related to respiratory events and/or snoring were selected for further investigations using a complete PSG. Five patients refused this second study and one patient with the highest esophageal pressure value recorded died of nonrespiratory cause before the second sleep study. Symptoms and findings of 21 patients entering PSG are reported in Table 3.

Table 2. Characteristics of 67 patients and results of LPG according to diagnosis (phase I) in snorers (study I). Unless otherwise indicated the data represent mean values, with standard deviation in parenthesis.

	OSA (n = 14)	Pes variations (n = 27)	Primary snoring (n = 20)	PLM (n = 6)
Age, yr	52 (11.2)	50 (8.7)	40 (6.5)	48 (6.9)
BMI, kg/m2	29 (6.2)	27 (3.7)	26 (4.3)	28 (5.5)
Female/male, n	2/12	7/20	5/15	0/6
Habitual snorers, n	12	24	15	4
Heavy snorers, n	12	23	13	5
Sleepiness (VAS, 0-100) %	43 (22)	53 (29)	51 (26)	48 (22)
Sleepiness score (0-24)	11 (4.7)	10 (5.5)	8 (4.6)	9 (1.9)
Limited polygraphic recording:				
ODI4	20.4 (9.4)	1.0 (1.0)	0.1 (0.3)	1.1 (1.6)
ODI4supine	28.7 (11.7)	2.0 (2.4)	0.2 (0.5)	3.0 (5.6)
ODI2.5	28.6 (11.5)	3.7 (2.7)	0.6 (0.7)	3.1 (2.5)
Snoring >60dB, min/h	26 (18)	11 (15)	10 (18)	10 (10)
Pes var, min/h	34.0*(19.9)	15.3 (14.7)	0.0	1.5 (2.3)

OSA: obstructive sleep apnea; PLM: periodic leg movements; BMI: body mass index; VAS: visual analogue scale; Habitual snoring: self-reported snoring every night or almost every night; Heavy snoring: history of very loud snoring; Sleepiness score: total score of sleepiness counted from the questionnaire and VAS; ODI4: number of oxygen desaturations >4% per hour in bed; Pes var: increased esophageal pressure variation.

Three of the 21 patients had no evidence of SDB by our criteria (AHI <5, RERAs <5) (Table 3). However, in the supine position one of them had a high AHI (30). They all reported heavy snoring and sleepiness on VAS and/or Sleepiness score, but ESS values were not elevated. These patients were thus classified as patients with primary snoring.

Five patients fulfilled our criteria for UAR (AHI<5 and RERAs ≥5) (Table 3 and Figure 4). All five had a history of significant daytime sleepiness. Four of them were sleepy according to the Sleepiness score and two patients with UAR finding had elevated ESS values. Only two patients had sleep latency less than 10 minutes (5.2 and 9.1) in MSLT. The patient with shortest sleep latency had OSA while supine (AHI 21).

PSG of the 21 patients revealed 13 (62%) new OSA diagnoses (AHI ≥5). OSA was mild in 8 patients (AHI 5-15), moderate in 4 patients (AHI 15-30) and severe in one patient (AHI>30) (STM 2002). Three OSA patients were

subjectively sleepy (ESS and/or Sleepiness score) and another 4 patients had mean sleep latency less than 10 minutes (4.1-9.5).

PSG revealed four patients with PLM index above 7 (10.4-46.4). They all had OSA. These patients were not excessively sleepy.

Table 3. Diagnosis, symptoms and findings of the 21 patients referred to PSG in phase II (study I). Unless otherwise indicated the data represent mean values, with range in parenthesis.

|	OSA (n=13)	UAR (n=5)	Primary snoring (n=3)
Age, yr	51 (36-68)	52 (41-59)	43 (36-59)
BMI, kg/m^2	27 (22-34)	26 (22-30)	28 (21-34)
Female/Male, n	3/10	2/3	1/2
Habitual snorers, n	12	5	2
Sleepiness (VAS, 0-100%)	46 (0-77)	63 (57-74)	82 (67-96)
Sleepiness score (0-24)	9.1 (1-20)	12.3 (8-16)	14.0 (8-17)
ESS (0-24)	8.1 (4-14)	8.2(3-14)	6.3 (4-10)
MSLT, min	11.3 (3.7-20.0)	9.5 (5.2-13.1)	15.3 (12.5-18.1)
Limited polygraphic recording:			
Pes var,min/h	17 (2-53)	11 (2-20)	7 (5-9)
Polysomnography:			
AHI	15.1 (5.3-31.6)	2.5 (0.2-4.4)	2.8 (2.3-3.6)
AHI supine	37.1 (7.3-94.9)	6.1 (0-21.2)	10.9 (0-30)
Arousals/h	18.7 (6.4-39.2)	16.7 (9.4-34.5)	8.7 (6.1-13.3)
RERAs/h		9.3 (6.0-19.4)	3.4-4.7

OSA: obstructive sleep apnea; UAR: upper airway resistance; BMI: body mass index; Habitual snoring: self-reported snoring every night or almost every night; VAS: visual analogue scale; Sleepiness score: total score of sleepiness counted from the questionnaire and VAS; ESS: Epworth sleepiness scale; MSLT: multiple sleep latency test; Pes var: increased esophageal pressure variation; AHI: apnea-hypopnea index; RERA: respiratory effort related arousal.

1.4 Increased esophageal pressure variation and OSA diagnosis (phases I and II)

Increased Pes in LPG was significantly related to the diagnosis of OSA obtained from either LPG or complete PSG. Increased Pes was also related to di-

agnosis of SRBD (p<0.001). Pes correlated with ODI4 (p<0.001). Increased Pes variation over 20min/h indicated OSA and over 10min/h indicated SRBD.

Figure 4. An UAR-finding on PSG: Esophageal pressure (Pes) nadir decreases and para-doxal thoraco-abdominal movements are seen. Flow decreases less than 50%. The episode ends to an arousal demonstrated as an abrupt shift in EEG frequency and increase of chin EMG activity. The patient slept on his back. Channels from top to bottom: left and right electro-oculogram, the 4 EEG channels, chin (submental) EMG, electrocardiogram (ECG), heart rate (RR), flow, Pes, abdominal and thoracic movements, microphone, oximetry (SpO$_2$), end tidal CO$_2$ (ET- CO$_2$) body position and left and right leg (tibial) EMG.
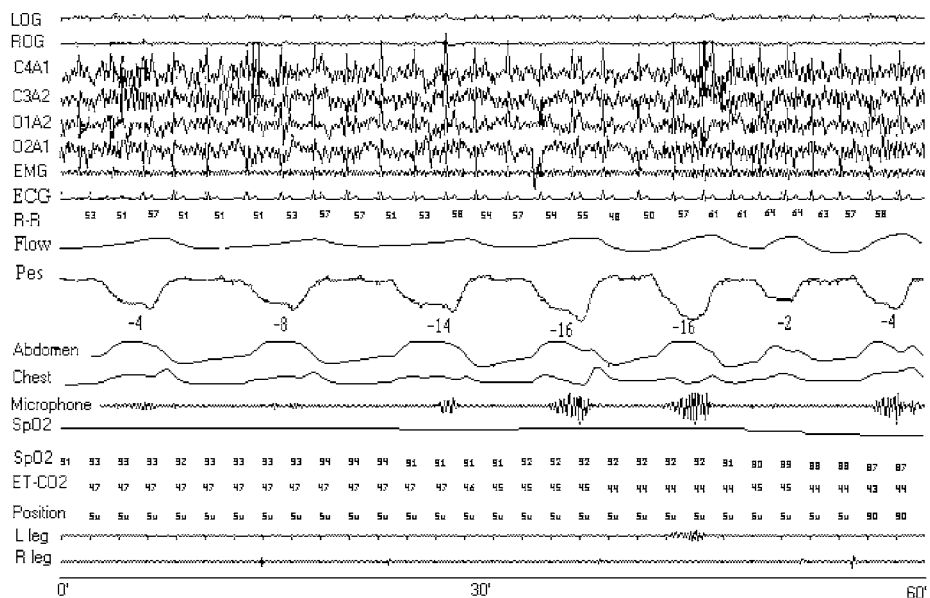
1.5 Snoring and sleep-related breathing disorders

History of intense and habitual (every night or almost every night) snoring was significantly associated with OSA (p=0.04). Snoring minutes correlated with Pes variation (p=0.01) and with ODI4 values (p=0.02). However, the total re-corded snoring minutes for OSA and UAR patients did not differ significantly as compared with other patients.

1.6 Position-dependent obstructive events

The ODI4 value increased while supine in both OSA and non-OSA patients, but the increase was significantly higher in OSA patients (p= 0.01). In all patients with abnormal Pes variation combined with desaturations while supine in LPG (ODI4supine ≥1) significant SRBD was found on further PSG.

1.7 Daytime sleepiness and sleep-related breathing disorders

In the patients undergoing PSG the ESS value showed excessive sleepiness in 4 patients and 9 patients were sleepy according to the Sleepiness score. Mean sleep latency was less than 10 minutes in 7 patients. Neither subjective nor objective measurements of sleepiness could predict OSA or UAR diagnosis. Nor could we find a correlation between Pes values and ESS or Sleepiness score.

1.8 The effect of esophageal pressure monitoring on nasal resistance (study II)

In the control measurements without nasal manipulation, the decongested unilateral nasal resistances of the nasal passages later introduced with transnasal catheter and of the contralateral nasal passages did not differ statistically. Only one patient had a slight structural unilateral obstruction according to our normal values for decongested mucosa. Mean nasal resistance values are presented in Figure 5.

On the catheter side, nasal resistance was increased with the catheter in place (mean UNR, 3.70) compared with the control measurement (mean UNR, 0.82) (p=0.01). After removal of the catheter, nasal resistance on catheter side (mean UNR, 0.96) did no longer differ significantly from the control measurement.

On the noncatheter side, nasal resistance with catheter in place (mean UNR, 0.75) and after removal of the catheter (mean UNR 0.86) was higher compared with control measurement (mean UNR 0.65), but this difference was not significant. Nasal resistance with catheter in place and after catheter removal did not differ significantly on this side.

TNR was not significantly different with the catheter (mean TNR, 0.44) or after removal of the catheter (mean TNR, 0.24) compared with the control measurement (mean TNR, 0.27). Nor was the corrected combined nasal resistance (mean TNR, 0.52) significantly increased compared to the control measurement without nasal manipulation.

Figure 5. Mean nasal airway resistance of 33 patients with transnasal catheter in place, after removal of the catheter and in the control recording. Corrected value of total nasal resistance with catheter in place is presented (study II).
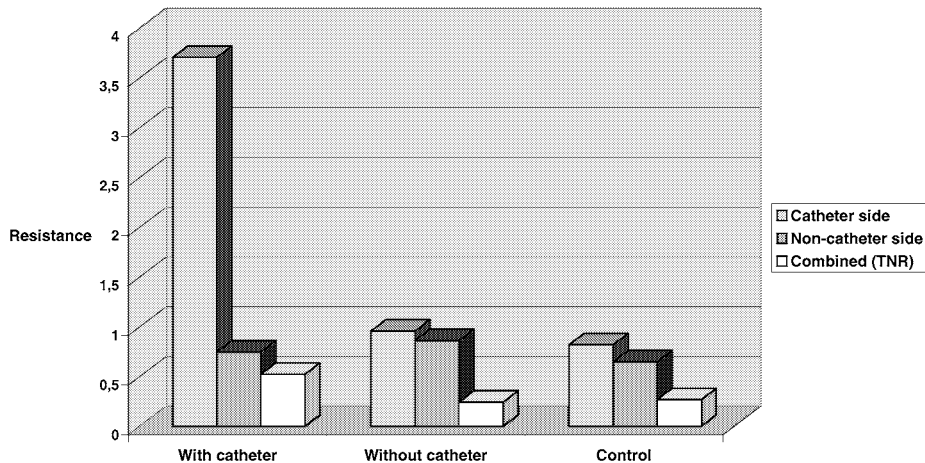
2 Positional and decongestive changes in nasal measurements (study III)

Patient characteristics and data on polysomnography in all patients and in non-obese and obese patients are shown in Table 1 and 4. Seventeen patients (mean age 46, range 29-62 years; mean BMI 29.7, range 26-37 kg/m^2) had AHI>10.

Total nasal resistance (TNR) increased on lying down for both patients and control subjects. The change in TNR after lying down or after decongestion did not differ between these groups (Table 5). In ARM nasal volumes decreased less after lying down and increased less after decongestion in the patient group compared with the control subjects (Table 6). When patients and control subjects with history of seasonal or perennial allergy and patients using nasal medication were excluded from the analysis, positional and decongestive changes in ARM remained lower in the patient group (p<0.05). TNR increased more on lying down in patients with OSA (AHI>10) compared with non-apneic control subjects (Table 5), but when patients with OSA were compared with control subjects, the difference was not statistically significant.

Table 4. Patient characteristics and PSG data in obese and non-obese groups of snorers (study III). The data represent mean values, with standard deviations in parenthesis.

	Patients with BMI< 30kg/m^2	Patients with BMI≥ 30kg/m^2
Subjects, n	29	12
Age, years	43 (9.0)	44 (9.1)
BMI, kg/m^2	26.4 (2.1)	32.3 (2.6)
AHI	7.9 (8.7)	27.5 (20.1)
ODI4	8.2 (10.1)	34.7 (23.0)
Sa02 <90%, %	1.8 (4.4)	12.6 (20.9)
TST, min	392 (62)	374 (112)
SE, %	83 (11)	79 (20)
WASO, min	57 (47)	74 (75)
SWS, %	16 (7)	11 (8)
REM sleep, %	18 (6)	17 (8)

BMI: body mass index; AHI: apnea-hypopnea index; ODI: oxygen desaturation index; Sa <90%: time with arterial oxygen saturation below 90%; TST: total sleep time; SE: sleep efficiency (TST/ time in bed); WASO: wake after sleep onset; SWS: slow wave sleep; REM: rapid eye movement.

Table 5. RMM data of snoring patients (study III). The data represent mean values, with standard deviations in parentheses.

	All patients	Controls	p	OSA (AHI>10)	Non-OSA (AHI<10)	p
Subjects, n	41	19		17	24	
TNR, Pa/cm^3/s						
Seated baseline	0.282 (0.195)	0.160 (0.070)	*	0.356 (0.255)	0.235 (0.131)	NS
Supine	0.371 (0.362)	0.230 (0.137)	NS	0.559 (0.481)	0.247 (0.176)	*
Decongested	0.220 (0.209)	0.097 (0.423)	*	0.284 (0.269)	0.174 (0.144)	NS
Postural effect, %	+38*	+43*	NS	+69*	+21	*
Decongestion effect, %	-21	-39**	NS	-16	-15	NS

TNR: total nasal resistance, Pa/cm^3/s; OSA: obstructive sleep apnea; AHI: apnea-hypopnea index; NS: not significant. All patients versus control subjects, OSA versus non-OSA , seated versus supine (postural effect) and seated versus decongested (decongestion effect) *: p<0.05; **: p<0.001.

Table 6. AR data of snoring patients (study III). The data represent mean values, with standard deviations in parentheses.

	All patients	Controls	p	OSA (AHI>10)	Non-OSA (AHI<10)	p
Seated baseline nasal volume,cm^3						
VOL 0-3	4.93 (0.82)	5.62 (1.60)	*	4.86 (0.81)	4.98 (0.84)	NS
VOL 2-4	4.03 (1.11)	5.30 (2.61)	*	3.79 (1.21)	4.19 (1.04)	NS
VOL 0-5	11.55 (2.47)	13.66 (5.06)	*	11.04 (2.80)	11.90 (2.23)	NS
Supine nasal volume, cm^3						
VOL 0-3	4.74 (0.89)	5.18 (1.00)	NS	4.43 (0.67)	4.94 (0.96)	NS
VOL 2-4	3.82 (1.39)	4.00 (1.16)	NS	3.23 (1.19)	4.19 (1.40)	*
VOL 0-5	10.95 (2.83)	11.25 (2.46)	NS	9.92 (2.60)	11.59 (2.83)	NS
Decongested nasal volume, cm^3						
VOL 0-3	5.54 (1.15)	6.74 (2.00)	*	5.38 (0.97)	5.65 (1.26)	NS
VOL 2-4	5.28 (1.52)	8.17 (3.09)	**	4.98 (1.28)	5.47 (1.65)	NS
VOL 0-5	13.53 (2.95)	18.53 (5.59)	**	12.82 (2.50)	13.99 (3.18)	NS
Postural effect, %						
VOL 0-3	-3	-8	NS	-7*	0	NS
VOL 2-4	-5	-25*	*	-14*	+3	NS
VOL 0-5	-5	-18*	*	-9*	-1	NS
Decongestion effect, %						
VOL 0-3	+12**	+20**	*	+10*	+14**	NS
VOL 2-4	+30**	+54**	**	+33*	+39**	NS
VOL 0-5	+17**	+36**	*	+17*	+21*	NS

OSA: obstructive sleep apnea; AHI: apnea-hypopnea index; NS: not significant. Patients versus control subjects, OSA versus non-OSA, seated versus supine measurements (postural effect) and seated versus decongested (decongestion effect) *: p<0.05, **: p<0.001.

3 Nasal obstruction and sleep-related breathing disorders (study III)

In the overall patient group nasal volumes in supine measurements correlated inversely with AHI (VOL 2-4, r=-0.32, p<0.05) (Figure 6) and with ODI4 (VOL 0-3, VOL 2-4,VOL 0-5, p<0.05) (see Study III Figure 2). In the non-obese patients TNR in supine position correlated positively with AHI (r=0.50,

63

p<0.05) (Figure 7) and ODI4 (r= 0.58, p<0.05) (see Study III Figure 4), and nasal volumes in supine measurements (VOL 2-4 and VOL 0-5) were inversely correlated with ODI4 (r= -0.41, r= -0.38, p<0.05). The change in nasal measurements on lying down (supine measurement subtracted from baseline seated measurement) correlated with AHI and ODI4 only for RMM in the non-obese group (r=-0.47, r=-0,48 respectively, p<0.05). No significant correlations were found between nasal resistance or volumes measured in a seated position and sleep parameters. Measurements after decongestion of the nasal mucosa correlated with ODI4 in non-obese patients for both RMM (r=0.45, p<0.05) and AR (VOL 2-4, r= -0.41, p<0.05; VOL 0-5, r= -0.38, p<0.05).

Figure 6. In the overall patient group nasal volume measured in supine position at distance 2-4cm from the nares (VOL 2-4) correlated inversely with AHI (r= -0.32, p<0.05).
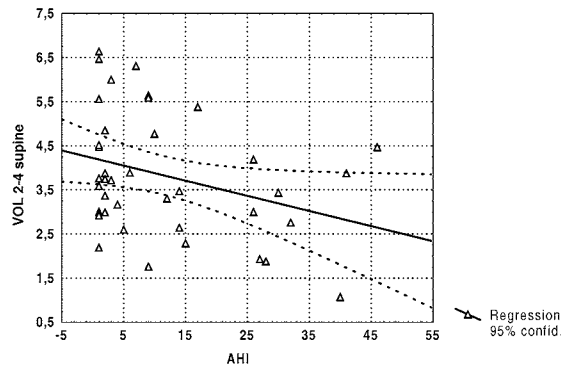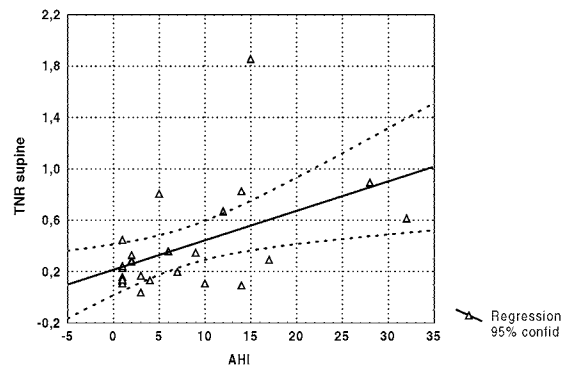

Figure 7. In the non-obese patients TNR measured in supine position correlated with AHI (r= 0.50, p<0.05).

4 Postural cephalometric analysis and nasal resistance in sleep-related breathing disorders (study IV)

The snoring patients were stratified according to BMI (BMI <30kg/m2 in non-obese patients) and selected cephalometric variables, facial angle divergence (sella-nasion/mandibular plane, SN/MP angle) and anteroposterior position of lower jaw (sella-nasion-supramentale, SNB angle), for comparison of subgroups. Patient characteristics, total nasal resistance of decongested mucosa and data on PSG in the subgroups are presented in Table 7. Corresponding data on the overall patient group in study IV is shown in Table 1.

Table 7. Patient characteristics and data on polysomnography and rhinomanometry by subgroups of snorers (study IV). The data represent mean values, with standard deviation in parenthesis.

	Non-obese BMI<30kg/m2	Obese BMI≥30kg/m2	S-N/MP ≥28.6º †	S-N/MP <28.6º †	SNB ≥78.3º †	SNB <78.3º †
Subjects, n	29	11	21	19	21	19
Age, years	44.5 (9.8)	43.6 (9.5)	47.1 (7.2)	41.1 (11.0)*	45.3 (9.3)	43.1 (10.0)
BMI, kg/m2	26.1 (2.0)	32.5 (2.7)	27.0 (3.6)	28.8 (3.4)	28.3 (3.4)	27.3 (3.8)
TNRdec, Pa/cm3/s	0.19 (0.18)	0.24 (0.12)	0.21 (0.20)	0.19 (0.11)	0.22 (0.21)	0.17 (0.07)
AHI	7.0 (7.9)	29.8 (19.3)**	9.7 (14.0)	17.2 (17.0)	14.0 (16.0)	12.4 (15.8)
SaO2 <90%, %	1.6 (4.2)	13.4 (21.8)	2.5 (6.4)	7.4 (17.2)	5.7 (16.2)	3.8 (7.8)

S-N/MP: facial angle divergence: the angle formed by sella (S)-nasion (N) line and mandibular plane (MP); SNB: antero-posterior position of lower jaw: the angle formed by S-N line and N-supramentale (B) line; † median; BMI: body mass index; TNRdec: total nasal resistance after decongestion; AHI: apnea/hypopnea index; SaO2<90%: time with arterial oxygen saturation below 90%; *$p<0.05$; **$p<0.001$, non-obese versus obese or high S-N/MP angle versus low S-N/MP angle or high SNB angle versus low SNB angle.

4.1 The effect of posture on cephalometric measurements

After lying down and after adoption of a relaxed mandibular position significant changes were found in the mandibular position, soft palate angle, tongue length and height, pharyngeal airway at the level of soft palate and tongue, as

well as in the position of the hyoid bone in the overall patient group. The 33 cephalometric skeletal and soft-tissue variables used in this study and comparisons of upright and supine measurements are presented in Table 8.

4.2 Mandibular position and pharyngeal airway

Lower jaw rotated downwards and posteriorly on lying down. Mean anterior facial height (N-ME) increased 3.4mm (SD 4.3). The change in mandibular position was related to several pharyngeal measurements. The difference of anterior facial height from upright to supine position (deltaN-ME) was found to be correlated with minimum distance from soft palate to posterior pharyngeal wall in the supine position (suve1-ve2) (r= 0.57, $p < 0.05$). The difference of facial angle was also significantly correlated with pharyngeal measurements: change in soft palate angle (deltaANS-PNS/PNS-u1) (r= 0.51, $p < 0.05$) and postural change in posterior airway space (deltapas1-pas2) (r= -0.46, $p < 0.05$).

4.3 Nasal resistance and cephalometric measurements

Nasal resistance was not related to changes in mandibular position. TNR after mucosal decongestion (TNRdec) was related to measurements at the level of the tongue especially in the non-obese patients. In this subgroup TNRdec after decongestion correlated positively with minimal pharyngeal airway space at the tongue base level (ph1-ph2) in both positions (r=0.53 upright, $p < 0.05$; r=0.61 supine, $p < 0.05$) and was in inverse relation with total tongue length in the supine position (suTant-va) (r= -0.48, $p < 0.05$). Accordingly, in the overall patient group nasal resistance in supine position (TNRsu) correlated positively with pharyngeal measures (supas1-pas2, r=0.39, $p < 0.05$; suph1-ph2, r=0.49, $p < 0.05$) and with the change in oral tongue length (deltaTant-Tgon, r=0.58, $p < 0.05$).

4.4 Obesity and pharyngeal measures

BMI correlated with thickness of uvula (sp1-sp2: r=0.31, $p < 0.05$) and length of the tongue in both positions (Tant-va: r=0.45; suTant-va: r=0.42, $p < 0.05$). BMI also correlated significantly with the distance of the hyoid bone from third cervical vertebra (H-C3) (r=0.51, $p < 0.05$) in the upright position and with the distance of the hyoid bone from the posterior mandibular symphysis in the supine position (suH-RGN) (r=0.50, $p < 0.05$).

Table 8. Cephalometric skeletal and soft-tissue measurements in the snoring male patients (study IV). The data represent mean values with standard deviations in parenthesis. Variables with significant changes in a supine position are shown.

Variables Distances (mm), angles (°)	Upright Mean (SD)	Supine Mean (SD)
Cranial measurements:		
Cranial base angle (S-N/S-BA)	130.2 (5.8)	-
Anterior cranial base (S-N)	71.1 (3.0)	-
Posterior cranial base (S-BA)	46.0 (3.9)	-
Facial skeletal measurements:		
SNA angle	82.6 (4.0)	
SNB angle	78.9 (4.4)	
ANB angle	3.7 (2.2)	
Anterior facial height (N-ME)	123.2 (8.6)	125.5 (9.8)**
Lower anterior facial height (ANS-ME)	70.8 (7.3)	-
Maxillary length (ANS-PNS)	55.0 (3.1)	-
Mandibular length (GN-CD)	119.5 (5.5)	-
Facial divergence (S-N/MP)	29.8 (8.2)	31.8 (8.4)**
Gonial angle (ME-GO inf/ART-GO post)	121.5 (8.2)	-
Craniocervical measurements:		
Craniocervical angle (NSL/CVT)	104.8 (8.7)	
NSL/VER angle	97.9 (6.9)	-
Soft palate:		
Soft palate length (PNS-u1)	40.1 (5.2)	
Soft palate thickness (sp1-sp2)	10.6 (1.6)	
Soft palate angle (ANS-PNS/PNS-u1)	125.9 (7.3)	132.4 (8.8)**
Tongue:		
Total tongue length (Tant-va)	78.0 (5.9)	73.3 (6.3)**
Oral length of the tongue (Tant-Tgon)	70.0 (5.7)	67.1 (5.6)**
Total tongue height (Tsup/Tant-va)	34.6 (4.0)	35.0 (3.2)*
Hyoid bone:		
H-MP	21.7 (6.0)	16.8 (5.5)**
H-PNS	74.5 (5.9)	
H/GN-C3	11.5 (6.6)	8.2 (6.8)*
H-C3	39.9 (3.5)	
H-RGN	38.9 (5.7)	33.1 (4.9)**
Pharyngeal airway:		
S-PNS	49.3 (3.4)	-

Variables	Upright	Supine
Distances (mm), angles (°)	Mean (SD)	Mean (SD)
AA-PNS	33.5 (6.5)	
PNS-ad1	24.3 (3.5)	
PNS-ad2	23.7 (3.8)	
ve1-ve2	6.6 (2.8)	3.3 (3.0)**
u1-u2	8.3 (3.0)	5.3 (3.9)**
pas1-pas2	10.5 (2.4)	
ph1-ph2	10.1 (2.9)	8.6 (3.6)*

Upright versus supine measurements *: $p<0.05$; **: $p<0.001$; n=34. Cephalometric points used for measurement of distances and angles are defined in study IV Figures 1 and 2.

5 Predictors of AHI in cephalometry, rhinometry and anthropometric data (study IV)

Twenty-one patients (53%) had AHI over 5. BMI correlated significantly with AHI (r=0.60, $p<0.05$). Linear correlations between AHI and cephalometric parameters are presented in Study IV Table 3 and results of stepwise regression models are shown in Table 9.

5.1 Regression model for the overall patient group

The stepwise regression analysis for all patients gave adjusted r^2 0.68 predicting that 68% of variation in AHI was explained by BMI and 3 cephalometric variables. BMI was the most significant predictor, followed by soft palate length (PNS-u1), hyoid position (H/GN-C3) and the distance of uvular tip from posterior pharyngeal wall in supine position (suu1-u2). As expected, high BMI, long soft palate, inferior position of hyoid bone and decrease in suu1-u2 were related to increased apneic activity (Table 9).

Table 9. Multiple stepwise regression in snoring patients with AHI as dependent variable (study IV).

	Beta	Standard error of beta	B	Standard error of B		p value
All patients					t (26)	
Intercept			-91.269	20.91	-4.364	<0.001
BMI	0.559	0.104	2.375	0.442	5.368	<0.001
PNS-u1	0.291	0.121	0.883	0.368	2.401	0.024
H/GN-C3	0.363	0.104	0.856	0.246	3.483	0.002
suu1-u2	-0.267	0.123	-1.111	0.514	-2.163	0.040
Non-obese patients					t (11)	
Intercept			-24.359	4.941	-4.930	<0.001
suph1-ph2	0.800	0.128	2.205	0.352	6.270	<0.001
deltaANB	-4.474	0.096	-1.812	0.368	-4.926	<0.001
TNRdec	-0.590	0.125	-23.973	5.088	-4.712	<0.001
suPNS-ad2	0.378	0.097	0.744	0.191	3.886	0.003
deltaH-MP	-0.253	0.099	-0.702	0.274	-2.562	0.026
Facial divergence (S-N/MP≥28.6°†)					t (13)	
Intercept			3.962	12.304	0.322	0.753
suH/MP	0.559	0.173	1.420	0.440	3.228	0.007
supas1-pas2	-0.420	0.173	-1.926	0.793	-2.427	0.030
Facial divergence (S-N/MP<28.6°†)					t (9)	
Intercept			-104.045	35.067	-2.967	0.016
BMI	0.791	0.092	3.728	0.435	8.561	<0.001
suTsup/Tant-va	-0.658	0.098	-4.155	0.620	-6.699	<0.001
S-BA	0.511	0.919	2.152	0.387	5.555	<0.001
supas1-pas2	0.366	0.093	1.679	0.425	3.948	0.003
Mandibular position (SNB≥78.3°†)					t (13)	
Intercept			-142.210	20.168	-7.051	<0.001
BMI	0.538	0.120	2.350	0.526	4.467	<0.001
PNS-u1	0.380	0.132	1.130	0.392	2.883	0.013
suH-C3	0.328	0.136	1.153	0.479	2.408	0.032
Mandibular position (SNB< 78.3°†)					t (11)	
Intercept			-51.371	25.920	-1.982	0.073
H-PNS	0.673	0.113	1.742	0.291	5.980	<0.001
u1-u2	-0.702	0.122	-3.549	0.617	5.752	<0.001
PNS-u1	-0.294	0.125	-0.915	0.389	-2.352	0.038

For all patients: r= 0,851, r^2adj= 0.681, p<0.001, F (4.26) = 17.016, standard error of estimate is 9.348. For non-obese patients: r= 0.949, r^2adj= 0.856, p< 0.001, F (5,11)=20.091, standard error of estimate is 3.206. For patients with S-N/MP≥28.6 degrees: r=0.816, r^2adj= 0.614, p<0.001, F (2.13) =12.924,

standard error of estimate is 8.519. For patients with S-N/MP<28.6 degrees: r= 0.966 , r^2adj= 0.896, p<0.001 , F (5.9) = 25.099, standard error of estimate is 5.745. For patients with SNB ≥78.3 degrees: r= 0.910, r^2adj= 0.788, p<0.001 , F (3.13) = 20.850, standard error of estimate is 8.055. For patients with SNB< 78.3 degrees: r= 0.932, r^2adj= 0.833, p<0.001, F (3.11) = 24.320, standard error of estimate is 6.275. † Median.

5.2 Model for non-obese patients

In the non-obese group, cephalometric parameters and nasal resistance explained 86% of the variation in AHI. Minimal pharyngeal airway space at the level of tongue base in the supine position (suph1-ph2) was the most important predictor. The difference in the antero-posterior position of the lower jaw after lying down (change in subspinale-nasion-supramentale angle, deltaANB) was the second variable explaining apneic activity. Nasal resistance followed by nasopharyngeal airway space in the supine position (suPNS-ad2) and the difference in the hyoid distance from mandibular plane after change of position (deltaH-MP) explained the residual variation in AHI. Removal of any one of the independent variables from the model significantly reduced the amount of explained variation. Increase in suph1-ph2 (r=0.36 NS), nasal resistance and suPNS-ad2 was related to increase in AHI. DeltaANB and deltaH-MP were inversely related to AHI indicating increased apneic tendency with opening of jaws in the supine position and with smaller decrease of H-MP when lying down. Suph1-ph2 correlated positively with difference in oral tongue length after lying down (r=0,47, p<0.05) and with TNR measured after decongestion (r=0,61, p<0.05). Although the Durbin-Watson test suggests that the residuals in this model were slightly autocorrelated, they were small. The obese subgroup was not large enough for prediction of sleep apnea.

5.3 Subgroups by facial divergence

For patients with a high facial angle (S-N/MP ≥ 28.6º, median) 61% of the variation in AHI was explained by supine measurements of the distance of the hyoid bone from mandibular plane (suH-MP) and the posterior airway space (supas1-pas2). Caudal position of the hyoid bone and decrease of supas1-pas2 (r= -0.58, p<0.05) were related to sleep apnea in this subgroup.

In the group with a low facial angle (S-N/MP< 28.6º), the model explained 90% the variation in AHI. The most important variable was BMI, followed by tongue height in the supine position (suTsup/Tant-va), S-BA and posterior airway space in supine position (supas1-pas2). Decreased tongue height in the supine position (suTsup/Tant-va) and increased S-BA distance and supas1-pas2 (r=0.35 NS) were related to sleep apnea.

5.4 Subgroups by anteroposterior position of lower jaw

The patients were divided into two subgroups based on the anteroposterior position of the lower jaw. In the group with SNB > 78.3°, the model explained 79% of variation in AHI. BMI was again the most important predictor, followed by soft palate length and the distance of the hyoid bone from the third cervical vertebra in the supine position (suH-C3). An increase in these measurements indicated higher apneic activity. SuH-C3 was significantly related to many pharyngeal measurements: suPNS-u1 (r=0.57), suPNS-ad1 (r=0,62), suPNS-ad2 (r=0.62), suTant-va (r=0.50), suH/GN-C3 (r=0.61)) ($p < 0.05$) and to natural head position (NSL/VER) (r=0.52)($p < 0.05$).

For patients with SNB < 78.3°, 83% of variation in AHI was explained by hyoid bone distance from PNS (H-PNS), the distance of uvular tip from posterior pharyngeal wall (u1-u2) and length of the soft palate. An increase in hyoid distance and soft palate length and a decrease in u1-u2 were related to OSA. Although the Durbin-Watson test suggests that the residuals in this model were slightly autocorrelated, they were small.

DISCUSSION

1 Methodological considerations

The patients in this study were snorers with wide range of BMI and age. However, obesity was not as common as in many other mainly nonsurgical clinical studies. This is because non-obese patients are regarded as suitable for consideration of operative care. Our sleep studies usually demonstrated mild SRBD or simple snoring. Mean TNR after decongestion was not higher in the study group waiting for operative care of nasal obstruction compared with snorers entering LPG with esophageal monitoring. However, in five patients RMM could not be performed due to obstruction of either nasal passage. The decision for operative care of nasal obstruction was based also on clinical findings and symptoms and not strictly by rhinomanometric criteria. In comparison with nonsnoring subjects both RMM and AR showed increased nasal obstruction in these snorers. However, there was a wide variation in nasal obstruction. The results of these patient samples can be considered representative of a clinical population referred to an otorhinolaryngology clinic for evaluation of snoring and possibly of a population with primarily an early stage of SRBD in general. Evaluation of nasal breathing using rhinometric measurements is necessary before decision of operative care.

The number of excluded recordings was high in the study evaluating esophageal monitoring in combination with LPG. This is because we applied strict criteria for acceptance of the esophageal recording, especially in nonapneic snorers, in the statistical analysis. The rejected recordings were still considered adequate to reach diagnosis for clinical purposes.

In the study of catheter effects on nasal resistance leakage of air was suspected after taping the nasal orifice of the catheter side. Therefore, measurement of unilateral nasal resistance of the non-catheter side after removal of the catheter was used to count a corrected TNR for catheter in place. Since measurements were performed right after another, error due to time interval or nasonasal reflex seems improbable.

In eight patients measurement of postural changes in TNR was not possible due to a severely obstructed nasal passage. This may be one reason for the lack of correlation between TNR and SRBD in the overall material. However, only two recordings failed in the obese group. In AR the narrowing of the structurally obstructed nasal passage may have impaired reliable measurements behind the obstructed site (Buenting et al 1994, Roithmann 1997b). AR has been reported to be at least as sensitive as RMM in the detection of postural and decongestive mucosal changes (Fouke and Jackson 1992), but this finding is

more likely to be true in subjects without significant structural nasal pathology. RMM and AR measure different aspects of nasal airways. In addition to the nasal dimensions measured in AR, the shape of the nasal passage will affect nasal airflow. RMM is a functional measurement of nasal breathing and may be anticipated to have a closer relationship with sleep parameters. However, the use of both methods was found complementary and gave support to the findings that postural nasal measurements, but not upright recordings, are associated with SRBD.

Growing recognition of postural changes in the soft tissue structures (Yildirim et al 1991, Pae et al 1994, Pracharctam 1994, Pae et al 1997, Pae et al 1999) and of the importance of the supine body position in apneic activity during sleep (Penzel et al 2001) have increased interest to investigate supine cephalometric analysis. Pae and his coworkers (1994) compared pharyngal airway measurements in upright and supine positions and found a stronger correlation for OSA in supine position. Accordingly, in the present study supine soft tissue measurements and position of hyoid bone were significantly associated with AHI. Supine variables and postural changes in these variables were also well represented in the models of subgroups possibly explaining the high predictive power for AHI in this study.

Cephalometry is a standardized radiographic method for upright evaluation of craniofacial structures (Scwab 2001). Advantages include low cost, availability and assessment of skeletal types, such as retrognathia. Comparison of upright and supine measurements is easy, but the method of the supine technique varies in different centers. The exposure is performed at end-expiration, at the phase when pharyngeal airway decreases to its minimum volume during the respiratory cycle, the time particularly vulnerable to collapse (Scwab et al 1993). MR imaging is more expensive, but excellent airway, soft tissue and fat resolution can be obtained. MR imaging studies are usually performed during tidal breathing and timing is more difficult due to the longer exposure time (Hiyama et al 2000). Higher variation in repeated measurements of the pharyngeal airway has been reported in MR imaging at the level of tongue. Studies of standardization of MR and CT imaging of the pharyngeal airway are few (Stuck et al 2002). Evaluation of factors in cephalometry influencing pharyngeal measurements and their relation with apneic activity may increase prediction of SRBD in upper airway imaging.

2 Esophageal pressure monitoring and limited polygraphic recording

The minimum proportion of SRBD in the snoring patients referred to our oto-rhinolaryngology clinic was 48%. Increased Pes variation combined with periodic breathing pattern predicted the diagnosis of OSA. An OSA finding was possible with only short periods of Pes variation in LPG. This may be due to variation of obstructed breathing between the study nights and somewhat different techniques. Therefore, finding of any increased Pes variations with periodic breathing movements and airflow should be considered indicative of a possible SRBD. The combination of Pes monitoring and periodic breathing variation with oximetry increased detected SRBD. Also previous studies have shown that oximetry alone is not an adequate method for screening purposes (Epstein et al 1998). Combination of detection of airflow and respiratory movements using SCSB and evaluation of periodic breathing has been shown to increase sensitivity of a limited sleeping study (Salmi et al 1989, Svanborg et al 1990).

The combined criteria of Pes variation and an increased ODI4 while supine in LPG suggested an SRBD diagnosis in phase II on PSG in this material. Collabsibility of the upper airways during sleep has been shown to be strongly dependent on body position (Penzel et al 2001). In many patients SRBD is more frequent in the supine position and may even be apparent only in the supine position, as we observed.

UAR was found in five of 21 patients referred on PSG and sleep latency on the multiple sleep latency test was clearly shortened in only one patient. However, MSLT has not been found to correlate with ESS scores in patients suspected of SRBD (Chervin et al 1999). Objective measurements of sleepiness are not necessary in the definition of OSAS and may be criticized in UARS. The finding of increase in apneas and hypopneas in supine position in UAR suggests the same pathophysiology as in OSA. Patients with excessive daytime sleepiness and increased Pes variation without signs of periodic changes in airflow and/or respiratory movement signal or periodic snoring were not found in this material. Although we did not investigate all our patients with PSG, it seems unlikely that UAR was missed in our LPG, since we used highly sensitive methods for detection of periodic breathing variation and a direct measure of respiratory effort. This study population was less symptomatic than patient samples in previous clinical studies on UARS. Part of our snorers were "social snorers" without other symptoms suggesting SRBD. In this center, patients with obesity and suspicion of severe OSA are usually referred to the pulmonary department. This may explain the lower number of patients with an UAR finding and daytime sleepiness (UARS) in the present study (Votteri et al 1994, Guilleminault 1995). On the other hand, UARS could be expected to be found in mainly non-obese snorers (Guilleminault et al 1993).

History of habitual and intense snoring was associated with OSA, but recorded snoring did not differ significantly between primary snorers and patients with SRBD. In our LPG studies continuous and periodic snoring were not quantified separately. Periodic snoring in OSA may have been underestimated by the number of snoring minutes.

At least 40% of these mainly non-obese snorers had OSA. SRBD was found in half of these snorers. Neither subjective nor objective measurements of sleepiness indicated a finding of OSA or UAR with acceptable accuracy. In addition to inter-individual susceptibility to sleepiness, the possible role of night-to-night variation of measured parameters, sleep fragmentation from non-respiratory causes and differing extent of disturbance caused by the respiratory events have been suggested to explain the poor association between sleepiness and respiratory related events (Stradling et al 2000). Therefore, daytime symptoms related to the findings of SRBD are emphasized as an indication for treatment. Moreover, a sleep study before operative care of snoring seems necessary.

PLMs were found in 10 of the patients (15%) referred to the sleep studies because of snoring. On PSG, four of our patients had both periodic leg movements and OSA. Sofar, the relationship between SRBD and PLM disorder is unclear (Chervin 2001, Ohayon and Roth 2002).

Eighty-seven percent of the patients in the present study had no contraindication for the insertion of the transnasal catheter and were able to carry on with it overnight. Compliance for the sleep study with esophageal monitoring was found good in this sample of snorers with mostly mild SRBD.

A transnasal catheter may potentially obstruct nasal breathing and lead to increase in SRBD. The variable effects of acute nasal obstruction on breathing during sleep have been demonstrated in earlier studies with nasal packing and in allergic rhinitis (Zwillich et al 1981, Olsen et al 1981, McNicholas et al 1982, Wetmore et al 1988, Millman et al 1996). Increase of sleep fragmentation has also been observed. In the present study a significant increase in unilateral nasal resistance of the catheter side was found. However, an increase of TNR with catheter use was not statistically significant in this material without major structural abnormalities in the nasal airways. Artificial nasal obstruction shown to have caused SRBDs in earlier reports was usually observed during total obstruction of both nasal passages. Partial unilateral nasal obstruction with catheter use is more probable in patients with patent nasal passages and it is likely to result in less significant changes in breathing during sleep. In patients with unilateral structural nasal obstruction, as in septum deviation, partial nasal obstruction may turn into total obstruction due to the cyclic change in nasal resistance (Cole 1989c). Additionally, the nasal inflammation, secretion and mechanical obstruction caused by the catheter and possibly postural changes exacerbated by the inflammation will contribute to nasal obstruction.

3 Positional and decongestive changes in nasal measurements

This study did not find an increase in positional or decongestive changes in nasal resistance or nasal volumes in the total clinical sample of snoring patients waiting for nasal surgery when compared with control subjects. In patients with OSA the postural change in RMM was increased compared with non-apneic snorers ($p<0.05$). The difference was not significant in comparison with the control subjects. However, the increase of mean TNR, 69%, on lying down was rather high in patients with OSA considering that over 30% changes have been regarded as pathological in previous studies (De Vito et al 2001).

Nocturnal nighttime symptoms of rhinitis, nasal congestion due to allergy and smoking have been associated with snoring or SRBD (Wetter et al 1994, Young 1997a, Young et al 2001). Recumbency increases nasal resistance and decreases nasal volume especially in acute or allergic rhinitis (Rundcrantz 1969, Hasegawa 1994). Additionally, nonspecific rhinitis and smoking have been associated with increased postural congestion (Stroud et al 1999). To date, studies on the causes of increased postural changes are few. Half of the patients complaining of regular nocturnal nasal congestion reported allergy as a cause of their symptom (Young et al 2001). Structural nasal abnormalities have also been associated with mucosal inflammation indicated by increased decongestive changes in RMM (Suonpää et al 1995). The lower decongestion effect in AR in the patient group compared with control subjects did not suggest such increased inflammation in these snorers scheduled for operative care of nasal obstruction. Although signs of nasal mucosal inflammation not related to symptoms of rhinitis have been reported in patients with OSA, the role of inflammation in the pathogenesis of OSA is unclear. Current smoking (49%) and, due to selection criteria, structural nasal deformity and habitual snoring were common findings in our patients. A slightly more common history of allergies in the control patients did not seem to affect our results of postural changes. Further studies of factors influencing postural changes, considering at least smoking, allergy testing, medication and structural abnormalities, are needed for a better understanding and treatment of nocturnal nasal congestion in snorers and patients with SRBD.

4 Correlation of nasal obstruction and sleep-related breathing disorders

In this study we have found significant linear correlations between nasal measurements performed in the supine position and sleep parameters. Previous studies have shown relationships between history of nasal stuffiness and snor-

ing (Stradling and Crosby 1991) and between measured nasal airflow and history of snoring (Young et al 1997a). However, only a weak relationship between total nasal resistance and AHI has been reported earlier. Nasal measurements in that study were carried out using posterior RMM in an upright position (Lofaso et al 2000). Recordings using posterior RMM in supine position were not predictive for OSA in a sample of snorers, and postural changes of the soft palate were considered to account for the higher nasal resistance values in the supine position in snorers compared with non-snoring control subjects (Desfonds et al 1997). Recently, the role of increased postural congestive changes in 36 patients with OSA was investigated using anterior RMM. AHI was not increased in patients with pathological postural RMM compared with the patients with small postural changes in nasal resistance (De Vito et al 2001). Our study had a different approach to this issue considering both structural and postural changes. Postural changes may vary in each individual, but the combination of both structural and congestive obstruction seemed to explain variation in both AHI and ODI. Our results are in agreement with several previous studies in that no significant correlations could be found between upright nasal measurements and SRBD in either RMM or AR (Blakley et al 1987, Lenders et al 1991, Stradling and Crosby 1991, Atkins et al 1994, Young et al 1997b).

The finding of a significant association only between supine nasal measurements and sleep parameters emphasizes the role of congestive changes in SRBD. In RMM of non-obese patients the change in nasal resistance on lying down was associated with the increase of apneic activity. It remains to be seen if nasal measurements in supine position are more useful in assessment of treatment results in snorers. Whether inadequate treatment of postural mucosal changes has some role in the limited efficacy of treatments of nasal obstruction in snoring and OSA will also need further evaluation.

Significant associations between sleep parameters and nasal volumes measured at distances 2-4cm and 0-5cm in supine position in ARM were found in the overall patient group. Associations found between ODI and nasal measurements after decongestion in RMM and AR indicate that structural abnormalities also contributed to the found relationships in this material.

Obesity is known to be a major contributing factor in OSA (Hoffstein and Szalai 1993). A significant positive correlation between AHI and BMI was found also in the present material. Since obesity as a strong contributor to OSA may be able to obscure interdependency between nasal obstruction and SRBD, the relationship was investigated in non-obese patients in separate. In accordance with this hypothesis, TNR in supine RMM correlated significantly with both AHI and ODI in the non-obese patients group. This finding of a stronger relationship between non-obese patients may also be related to the less severe sleep disorder found in this group or maybe to the amount of oral breathing in

this group. Increase in oral breathing, not investigated in this study, may diminish the effect of nasal obstruction in moderate and severe forms of OSA. A recent report on frequency of mouth breathing found no increase in oral breathing in groups with more severe OSA (Oeverland et al 2002).

Nasal obstruction is considered to be one of the modifiable risk factors in OSA among obesity and smoking. If confirmed by other studies, the results of the present study support the concept of early treatment of nasal obstruction in primary and secondary prevention of OSA.

5 Postural cephalometric analysis, nasal resistance and anthropometric data in sleep-related breathing disorders

A change of body position from upright to supine with voluntary relaxation of the mandible decreased pharyngeal airway space and changed the position of soft palate, tongue and hyoid bone. Hyoid bone moved anteriorly and cranially after postural change. Lower position in supine position seemed to be related to increased apneic activity. This may reflect increased need for compensatory mechanisms to maintain a patent airway. The tongue changes its shape and has been found to sink down (Pae et al 1999). Decrease in pharyngeal airway patency after assuming supine position during wakefulness has been demonstrated earlier in most studies of normal subjects and patients with OSA using cephalometry and acoustic reflection technique, although findings at the retrolingual airway have varied (Yildirim et al 1991, Pae et al 1994, Martin et al 1997b, Fouke and Strohl 1987, Fransson et al 2002).

The relaxation of the mandible on lying down was observed as an increase in facial angle and anterior facial height. The change was nearly equal to the increase in facial height of normal subjects after falling asleep when compared with supine position with teeth in occlusion during wakefulness (Hiyama et al 2000). Opening of mouth increases upper airway collapsibility in normal sleeping subjects (Meurice et al 1996). Only an arbitrary sleep-like relaxation of mandibular position may be expected from an awake rest position, since jaw opening has been demonstrated to vary during the respiratory cycle in sleep and in different sleep stages (Hollowell and Suratt 1991, Miyamoto et al 1998).

Opening of jaws on lying down was significantly associated with decrease of pharyngeal airway space at both velopharyngeal and tonguebase levels. Concomitant change in body position affected pharyngeal airway dimensions, but can not explain the observed relationship. In the multiple stepwise regression analysis of non-obese subjects the voluntary change into mandibular rest position, in particular the variable presenting the anteroposterior movement of

the lower jaw, was found to be an independent predictor of AHI. These findings suggest, that the amount of jaw opening during mandibular relaxation obtained by these snorers may be proportional to the effects of jaw opening on pharyngeal patency during sleep. However, such a result will need confirmation by other studies and investigation of repeatability of the mandibular rest position.

Measurements of nasal resistance correlated significantly with pharyngeal airway measurements at the base of the tongue and with tongue length suggesting that increased nasal resistance was related to widening of the retrolingual airway and shortening of the tongue. The association was found in both upright and supine cephalometry. BMI or changes in end-expiratory mandibular position could not explain the association. A possible explanation for this finding could be the change from nasal to oronasal breathing in patient with high nasal resistance. Nasal resistance was not associated with opening of the jaws after lying down. Mouth breathing would have to have happened by opening of the lips and in upright position by maintaining occlusion of the teeth. Although nasal and oral breathing has been investigated by imaging with fluoroscopy and CT, little is known about tongue movements on assumption of mouth breathing (Stanford et al 1988, Rodenstein and Stanescu 1984). However, in two of eight healthy volunteers studied in upright posture using fluoroscopy a ventral and caudal movement of the tongue was observed, when a nose clip preventing nasal breathing was applied (Rodenstein and Stanescu 1984). If this will turn out to be the correct explanation for our findings in future studies, control of breathing route in upright and supine cephalometric studies evaluating soft-tissue measurements at the tongue-base level seems important.

Another explanation for the association of nasal resistance and tongue posture is the local control of pharyngeal dilator activity and the effect of nasal resistance on it. The dilator muscle activity and possibly also the augmented dilator muscle activity in patients with OSA is believed to be regulated by topical receptors (Mezzanotte et al 1992, Fogel et al 2000, Malhotra et al 2000). A switch from nasal breathing to stomal breathing in previously tracheostomized patients with OSA has been demonstrated to lead to a substantial decrease in genioglossal EMG activity (Malhotra et al 2000). The nature of stimulation and the location of these local receptors is so far unclear, but nasal receptors may also be involved (Horner et al 1991, Fogel et al 2000). Increased nasal resistance may be hypothesized to contribute to the awake genioglossal activity by nasal receptors or by decrease of negative pharyngeal pressure. This possible explanation for the relationship found in this study between tongue posture and TNR might affect airway measurements at the level of tongue in imaging studies of patients with SRBD in both upright and supine measurements.

In the non-obese patients minimal pharyngeal airspace in supine position (suph1-ph2) was found to be the most important variable predicting AHI in a model with high predictive power. This variable encompasses its relationship with nasal resistance. Moreover, TNRdec was found to be an independent contributor to AHI in this subgroup explaining apneic activity by some additional mechanism. Although the mechanisms remain to be explored, nasal resistance and its relationship with tongue position during wakefulness seems to have importance in prediction of SRBD in non-obese patients with less severe OSA.

In the overall material BMI was the main variable explaining AHI followed by soft palate length and a variable reflecting vertical position of hyoid. BMI was the most important contributor of SRBD in skeletal subgroups with prognathic mandible and low facial angle presenting craniofacial types not commonly related with OSA. This is in agreement with the recent report, in which BMI was found to be a relatively more important predictor of AHI in subjects with a larger anteroposterior facial dimension compared with subjects with a small anteroposterior facial dimension (Dempsey et al 2002).

Skeletal features have been demonstrated to influence the level of collapse in the passive pharynx of patients with SRBD (Wanatabe et al 2002). In the present study, in patients with low facial angle variables related to tongue position in the supine position and dimensions of the skull seemed to influence AHI second to BMI. This may reflect the maintenance of an upright tongue posture on lying down during wakefulness in patients with susceptibility to airway obstruction during sleep (Miyamoto et al 1997) and perhaps the relative importance of the tongue size and posture in relation to the skeletal boundary in this subgroup. In patients with a more retrognathic mandible and high facial angle the cranio-caudal position of the hyoid bone was the main variable predicting apneic activity. Hyoid position is considered to reflect susceptibility to collapse at the tonguebase (Millman et al 2000). BMI and cephalometric measurements gave high predictive power of SRBD in all skeletal subgroups, except in patients with high facial angle. Long face has been associated with narrow facial structure (Enlow 1996). It is probable that lateral pharyngeal soft- tissue and tonsillar size are relatively more important in these patients. Increase in airway space at the level of tongue in supine position seemed to be related with increase in AHI in patients with low facial divergence and in the non-obese patients with less severe sleep disorder, whereas decrease in airway space at this level was associated to increase in AHI in patients with high facial divergence. The ability to maintain airway patency during wakefulness may be different in the skeletal subtypes. The augmented genioglossal activity shown in earlier studies in patients with OSA (Mezzanotte et al 1992) and differences in compensatory abilities in different skeletal subgroups may make airway measurements at the level of tongue unpredictable especially in unselected patients. The role of skeletal subtype in awake pharyngeal postural changes has

been insufficiently investigated to date (Lowe et al 1996, Ono et al 1996, Dempsey et al 2002). Further studies will be needed using a greater number of patients.

Higher predictive power of AHI in the subgroups of BMI and skeletal subtypes suggests that several subtypes of OSA exist and they may have different contributing factors. In the future, a better definition of these subgroups in OSA may improve prediction of outcome in the surgical treatment of snorers.

CONCLUSIONS

I Sleep-related breathing disorders were found in 48% of snoring patients. At least 40% had a finding of obstructive sleep apnea, but upper airway resistance syndrome was not common among these patients. Periodic limb movements were a frequent finding.

II Increased esophageal pressure variation was significantly related with obstructive sleep apnea diagnosis. Increased esophageal pressure variation combined with any increase of oxygen desaturation index (ODI4) while the patient was in supine position predicted sleep-related breathing disorders in this material. Interference of the catheter on total respiratory airway resistance by increase of nasal obstruction is improbable in patients without major structural abnormalities in the nasal passages. Patient compliance of esophageal pressure monitoring (87%) was good considering the semi-invasiveness of the method.

III Neither postural nor decongestive changes in nasal measurements were increased in all snorers compared with control subjects. The postural changes found in patients with obstructive sleep apnea as compared with non-apneic snorers, as well as, causes of increased postural changes in nasal measurements will need further evaluation.

IV Significant linear correlations were found between nasal measurements measured with rhinomanometry and acoustic rhinometry in the supine position, and sleep parameters suggesting that nasal obstruction is a contributor to airway collapse. Postural congestive changes in nasal measurements were important in explaining the relationship between nasal obstruction and obstructive sleep apnea in these snorers. The association between nasal obstruction and sleep-related breathing disorders may be stronger in non-obese patients with less severe sleep apnea.

V A change of body position from upright to supine with voluntary relaxation of the mandible was associated with decrease in pharyngeal airway space and changes in position of soft tissue structures and hyoid bone. Findings of the present study suggest that nasal resistance and mandibular position may influence pharyngeal airway measurements in the supine position during wakefulness. Further investigation of the repeatability of a voluntary relaxed mandibular position and standardization of supine cephalometry is warranted.

VI Total nasal resistance after nasal decongestion and the change into a relaxed mandibular position were found to be independent predictors of apnea-hypopnea index in the group of non-obese patients. A relaxed man-

dibular position may show to improve prediction of apnea-hypopnea in-dex in imaging studies of snoring patients. The finding of high predictive power in several subgroups compared with the overall material suggests that several subtypes of sleep-related breathing disorders with different contributing factors can be found. Supine cephalometric analysis will need further investigation with consideration of mandibular position and evaluation of best predictors of sleep-related breathing disorders in vari-ous subgroups.

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