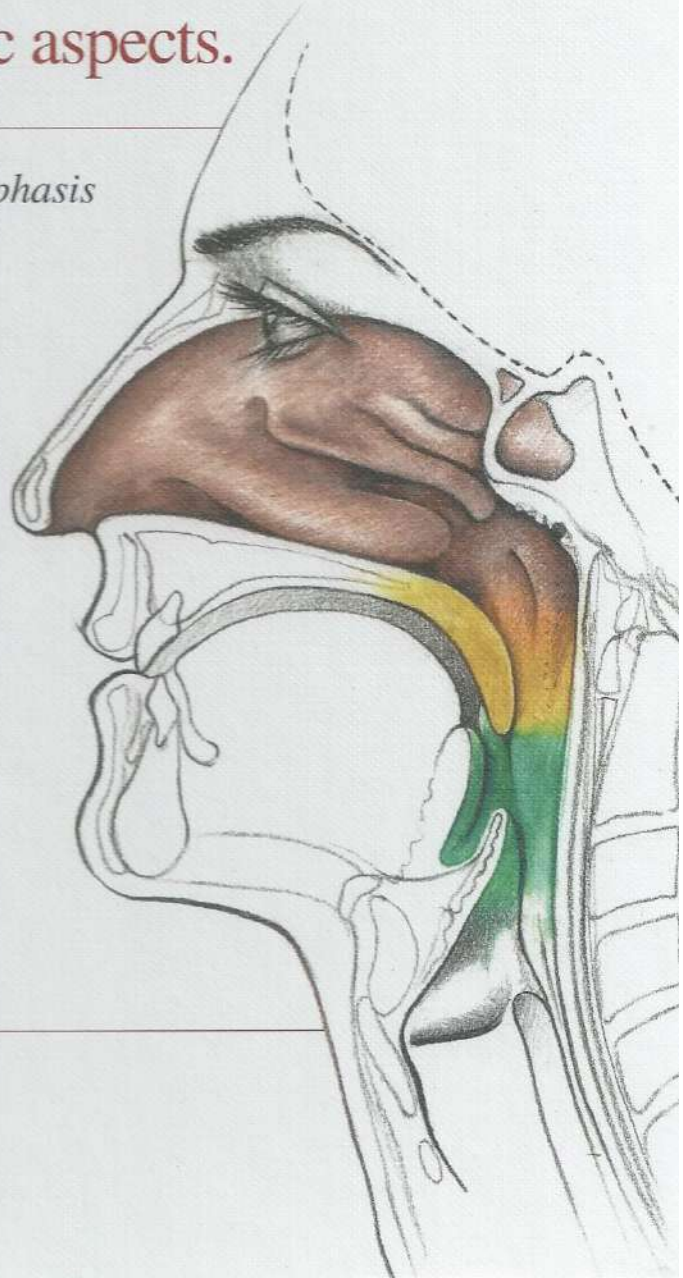
Snoring and obstructive sleep apnea syndrome: diagnostic and therapeutic aspects.

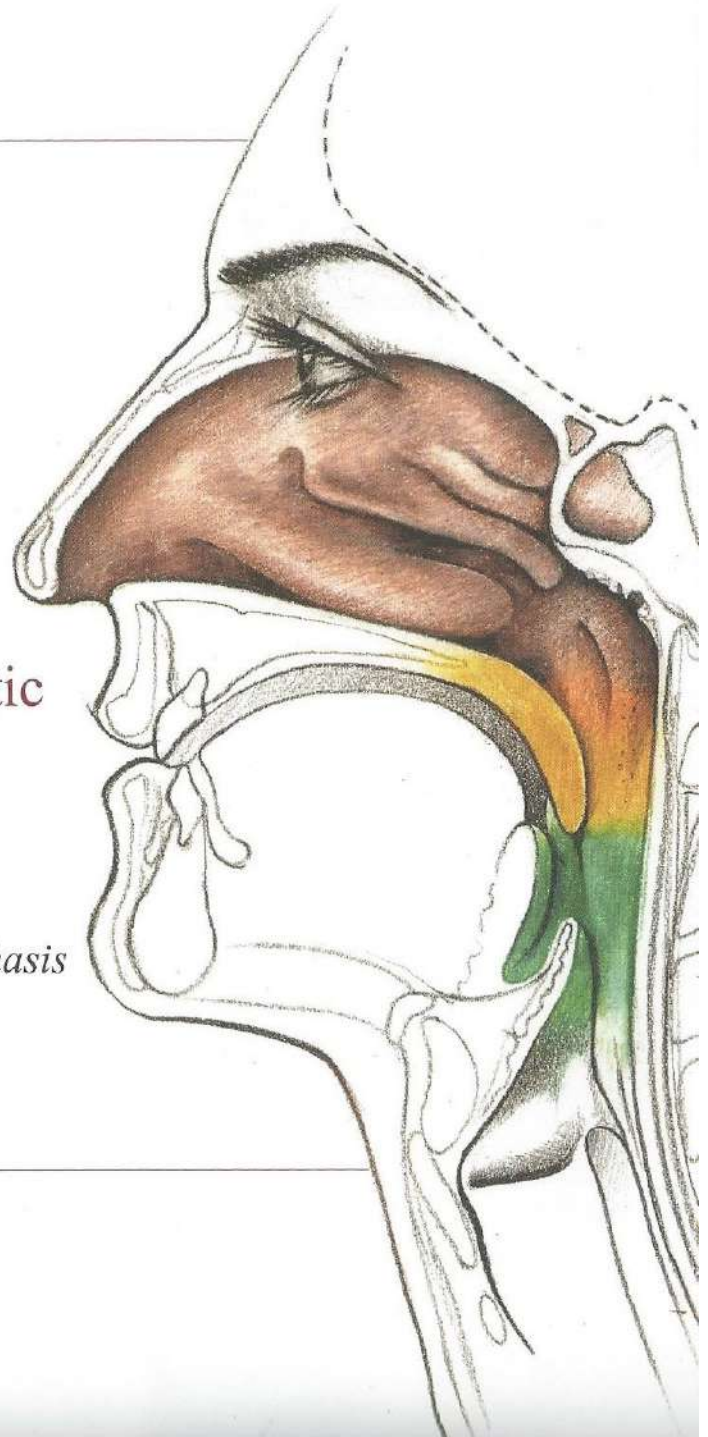
With special emphasis on UPPP



N.S. Hessel

Snoring and obstructive sleep apnea syndrome: diagnostic and therapeutic aspects.

With special emphasis on UPPP



N.S. Hessel

VRIJE UNIVERSITEIT

Snoring and obstructive sleep apnea syndrome: diagnostic and therapeutic aspects

With special emphasis on UPPP

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. T. Sminia,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de faculteit der Geneeskunde
op woensdag 2 juni 2004 om 13.45 uur
in het auditorium van de universiteit,
De Boelelaan 1105

door

Natascha Serena Hessel

geboren te Breda

promotor: prof.dr. C.R. Leemans
copromotor: dr. N. de Vries

Aan mijn ouders

Contents

Chapter 1

General Introduction

Historical Perspectives

No reason is known why males snore more than females, but an old legend held that primitive men defended their women even at night, by making terrifying noises to frighten away beast of prey. (1) This theory is now regarded as obsolete.

In the ancient Greek period the relation between sleep and sleep disorders was already discussed. Aelianus and Athenaeus described Dionysius, an obese sleepy man, "who choked in his own fat". It was impossible to awake him, unless long needles were stuck into his body. Breathing during his sleep was so difficult, that physicians ordered the attendants of Dionysius, to use the needles regularly to keep him breathing. (2)

In the English literature, William Shakespeare described four centuries ago in Prince Henry the clinical picture of (at least) socially unacceptable snoring:

"Falstaff: Now, Hal, what time of day is it, lad?
Prince Henry: Thou art so fat-witted, with drinking of old sack, and unbuttoning thee after supper, and sleeping upon benches after noon..."
ACT I, Scene II
Poins; "Falstaff! - Fast asleep behind the arras, and snoring like a horse.
Prince Henry: Hark, how hard he fetches breath..."
Act II, scene IV
King Henry IV Part I (3).

Another description in the English literature of a man with the sleep apnea syndrome is Joe, the fat boy, a character in the "The Posthumous Papers of the Pickwick Club" from Charles Dickens. (4) Joe's main activities are eating and sleeping. He is a loud snorer and hard to get awake. He has a red face (polycythemia) and his body is swollen (oedema, decompensatio cordis); his character is a kind of bizarre. The main character in the book, Samuel Pickwick, is obese but he has no signs of the sleep apnea syndrome. Dickens describes in an excellent way the effects of alcohol: "The wine had exerted its somniferous influence upon the senses of Mr. Pickwick. His head sunk upon his bosom; perpetual snoring and a partial choke occasionally, were the only audible indications of this great man's presence".

The first specification in the medical literature of the sleep apnea syndrome as a sleep disorder in an obese adult appears as late as 1966. (5) In 1972 at a congress in Italy, the relationship between hypersomnia and disturbed breathing during sleep was for the first time presented in scientific papers. (6)

Since then, an enormous amount of literature has been devoted to the subject. We now know that snoring can occur as only complaint, but that it can also be a manifestation of the obstructive sleep apnea syndrome. Research has focussed on many aspects of the syndrome, such as the incidence, pathophysiology, the local and general causes, the classical clinical picture, morbidity and mortality, how to establish the diagnosis and the various treatment options. This field of research has rapidly developed into one of the new challenges of modern medicine in general and of clinical neurophysiology, pulmonology and otolaryngology in particular. Obstructive sleep apnea is due to obstruction in the upper airway, while many general factors contribute to its development. Because of the obstruction in the upper airway, the otolaryngologist plays a central role in its diagnosis and treatment.

Obstructive sleep apnea syndrome

Snoring can be a social as well as a medical problem. There is a continuum of no snoring, occasional snoring, socially unacceptable snoring to snoring as manifestation of obstructive sleep apnea. The most advanced state of snoring is there-fore obstructive sleep apnea syndrome (OSAS) which may cause profound cardiac, pulmonary and behavioural problems. Apnea comes from the Greek term meaning "want of breath". Whereas snoring is caused by partial obstruction of the airway and fibrillation of parts of the upper airway, apnea means total obstruction. It interrupts the loud snoring with episodes of silence during which time the snorer struggles with unsuccessful respiratory efforts (obstructive apnea) to resolve the upper airway collapse.

Another common phenomenon in sleep apneic patients is not complete obstruction of the airway, in which still some air squeaks through. The event is called hypopnea or a hypopneic episode, when such airflow is reduced to less than 50 % of normal. Brief occasional obstructive events are harmless and are quite common in the normal adult population. Obstructive events are considered pathological when apnea episodes last over 10 seconds and occur over 7-10 times per hour (or 30 times per night). (7) This is often accompanied by kicking or flailing of the arms, or a body spasm. Sometimes events with sleepwalking with typical features of confusion and disorientation are mentioned. (8) These snorts and body motions often lead to spouses sleeping in different sleeping quarters.

Obstructive apneas are regularly accompanied with oxygen desaturations below 90 %. The compensatory tachypnea, which occurs after the apnea, causes an unstable breathing with strong variations in carbon dioxide tension (PaCO2). In the long run disturbances in the hormone regulation and excessive daytime sleepiness (hypersomnolence) may arise, because normal nocturnal recovery fails to occur. Other daytime symptoms caused by OSAS are retrograde amnesia, in ability to concentrate, personality changes and abnormal behavioural outburst, sexual problems and headaches. (7) OSAS can thus result in serious problems in private and professional life. Overall, quality of life can be severely affected.

Sleep related breathing disorders: definitions

Different names and definitions have been used through the years to describe the various sleep related breathing disorders. There is as yet no broad consensus regarding standard definitions. However, an American Academy of Sleep Medicine (AASM) taskforce report has addressed these issues in an attempt to come to generally acceptance of standards. (9)

Apnea is a cessation of airflow, exceeding 10 seconds.

There is no standard definition of *hypopnea*. Some define hypopnea as reduction of airflow to less than 50 % of normal. In another definition, hypopnea is defined as a reduction in airflow or respiratory effort for more than 10 seconds accompanied by oxygen desaturation of 3% or more and/or electroencephalographic evidence of arousal. (9,10)

There is also no consensus on the definition for obstructive sleep apnea syndrome, including thresholds. (7) The *apnea-hypopnea index (AHI)* is the number of apneas and hypopneas per hour of sleep and is used more or less interchangeably with the term *respiratory disturbance index (RDI)*. In one definition, an apnea-hypopnea index (AHI) between 5 and 15 apneas or hypopneas per hour combined with daytime sleepiness establishes OSAS (11). In another definition, only the AHI is used (occurrence of daytime sleepiness is not included). In this definition mild OSAS is: AHI between 15 and 20, moderate OSAS is AHI between 20 and 30, and an AHI > than 30 is regarded as severe OSAS. In this thesis this definition is used. However, others feel that the magnitude of associated symptoms and hypoxeamia also needs to be considered when severity is determined. (12)

Apnea can be obstructive, central of mixed. In obstructive sleep apnea, apneas are characterised by persistent respiratory effort without airflow, while with central apnea, respiratory effort is absent.

Central sleep apnea syndrome is characterised by cessation or decrease of ventilatory effort during sleep caused by failing central control of respiration, usually resulting in oxygen desaturation. Frequent awakenings and arousal with a sense of choking generally disturb sleep. Cardiovascular disease, cerebrovascular disease and other neurological damage affect the central control of respiration.

Upper airway resistance syndrome: This syndrome is not characterised by apneas or hypopneas, but caused by the changing high resistance of breathing during sleep, which causes recurrent tension of the lateral hypopharyngeal wall dilatory muscles. These patients exhibit all the daytime features of OSAS but have few apneas or hypopneas. Some of these habitual snorers have been found to have recurrent arousals from sleep, resulting from increases in upper airway resistance.

Central alveolar hypoventilation syndrome: This is a condition in which the alveolar ventilation is insufficient to fulfil the daily metabolic requirements. This disorder occurs in patients with normal mechanical properties of the lung. Causes of this type of hypoventilation are insufficient ventilation capacity (disorders affecting the chest and respiratory muscles), insufficient ventilation drive (disorders of the central nervous system, severe metabolic alkaloses, medication, narcotics and sedatives) and mixed forms such as the obesity hypoventilation syndrome, myxoedema and COPD (chronic obstructive pulmonary disease). In the case of insufficient ventilation drive, there can be a reduced sensitivity to increased CO2, which in primary form is caused by a lesion of the medullary chemoreceptors, while brainstem lesions after infarction, trauma or infection are found in secondary forms.

Obesitas hypoventilation syndrome(OHS): A synonym is the 'Pickwickian syndrome'. This form is characterised by obesity and chronic hypercapnia. There is often a combination of COPD with restrictive reduced lung capacity as a result from severe obesity and an unstable cardiorespiratory regulation mechanism.

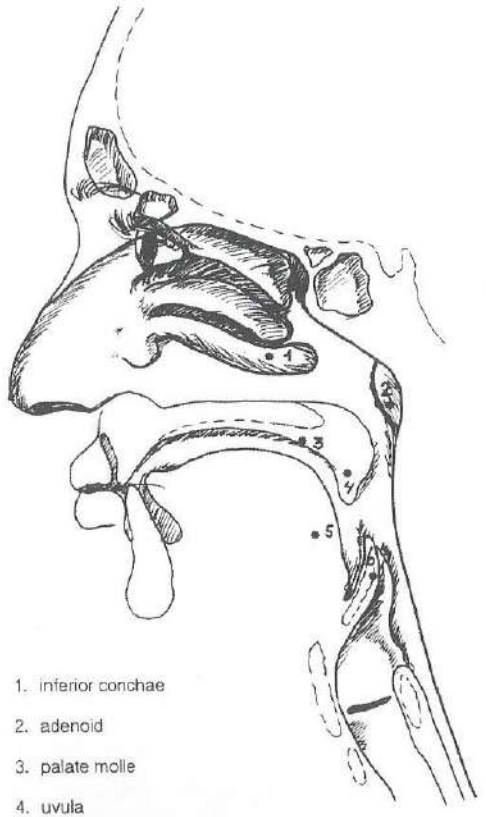
Prevalence of obstructive sleep apnea syndrome

Snoring is a general problem that is present in up to 24% of men and 14% of women. (13,14) With increasing age, this percentage rises to 60 % of men and 40% of women by age 60. Only a minority of snoring patients is seeking medical advise. It is estimated that OSAS affects 1.1 % of the Dutch population (15), and another estimation is that 80% of obstructive sleep apnea patients are not diagnosed. In a study of sleep registration in a population seeking medical attention for their snoring complaint in an ear, nose and throat practice it was found that 46.7 % of these patients had OSAS. (16)

OSAS prevalence has been investigated in few populations other than those of Western nations, and therefore the worldwide incidence of OSAS, as well as potentially important racial or ethnic patterns, are not yet clear. At present, data from studies of other people than Caucasians are too sparse even to determine with confidence if prevalence differs worldwide. (16) Population based studies suggest that OSAS prevalence is as high or higher in African-Americans as compared to Caucasians. (17)

Pathophysiology

The sound of snoring originates in the collapsible part of the upper airway where there is no rigid support. Usually such a narrow, floppy airway does not cause problems during wakefulness. During sleep the associated loss of skeletal muscle tone makes the upper airway narrower and floppier, particularly during rapid eye movement (REM) sleep when muscle relaxation is profound. The potential collapsible part reaches from the choanae to the epiglottis. It involves the soft palate, uvula, tonsils, tonsillar pillars, base of the tongue, and lateral pharyngeal muscles and mucosa. (Fig.1.)



1. inferior conchae
2. adenoid
3. palate molle
4. uvula
5. base of the tongue
6. epiglottis

Fig. 1

Both congenital and acquired forms of obstruction exist. Several factors, either single or in combination, contribute to snoring and in the worst cases lead to the development of OSAS.

Incompetent tone of palatal, lingual, and pharyngeal muscles play an important role. In deep sleepstages (in particular during REM-phase), these muscles fail to participate in the respiratory cycle to keep the airway open during inspiration. Specifically the dilator effect of the pharyngeal muscles and the protrusive effect of the genioglossus muscle are inadequate. (18,19) Thus the tongue falls backward into the airway and vibrates against the soft palate, uvula, and posterior and lateral pharyngeal folds.This is exaggerated when the person has consumed alcoholic beverages, sedative-hypnotics, or tranquillisers before retiring. Endocrine and metabolic disturbances, neuromuscular disorders, connective tissue disorders and storage diseases can also contribute to poor muscle tone, snoring, and apnea.

Space-occupying masses impinging on the airway can contribute to snoring. In children, snoring is almost always due to enlarged tonsils and adenoids. Approximately one-third of adults has tonsils large enough to contribute to the airway problem. (20) Bulky parapharyngeal tissues, due to fat deposition in the lateral pharyngeal walls, usually play an important role in obese persons. A receding chin may be unable to keep the tongue sufficiently forward. Retro- or micrognathia produces a tongue that is large relative to the space available for it to occupy. Patients with Down`s syndrome and acromegaly have an absolute tongue enlargement (macroglossia). Excessive length of the soft palate and uvula narrows the nasopharyngeal aperture, because the palate descends not only inferiorly in direction, but posteriorly as well.

Restriction of airflow in the nose (due to septal deviation, hypertrophic inferior turbinates, chronic nasal congestion due to allergic rhinitis, concha bullosa, paradoxically bent middle turbinates, polypoid middle turbinates, nasal polyps) creates increased negative pressure during inspiration which draws together the flaccid tissues in the collapsible part of the airway, where they vibrate and cause snoring, and sometimes hypopnea and apnea. This explains why many persons who ordinarily do not snore may do so when they have a cold or an allergic attack. Nasal obstruction is only one component of the etiology of obstructive sleep apnea and medical or surgical improvement of decreased nasal passage alone will not cure the majority of patients with moderate or severe OSAS. Still, the impact of a narrow nasal airway can be significant due to an increase in the velocity of airflow through the nose and thus increasing the collapse of the airway through Bernouilli's forces. (21-23)

Morbidity and Mortality

There are many sequelae of obstructive sleep apnea. There is evidence that a variety of confounding factors exists. (24,25) Heavy snorers are more likely to be hypertensive, and to suffer strokes and angina pectoris, than non-snorers of a similar age and weight. (26,27)

In the group of patients with obstructive sleep apnea there are more profound cardiac arrhythmia, pulmonary hypertension, behavioural problems and depressions. The risk of myocardial infarction is 23 times higher for men with obstructive sleep apnea (over 5.3 episodes per hour) than for comparable non-apneic men. (28) Repetitive hypoxemia in severe apneics contributes to general intellectual deterioration (impairment of verbal fluency, attention, memory, and executive functions) which may not be fully reversible. (29)

Systemic hypertension occurs in 40-60 % of OSAS patients, with a correlation to the severity of the obstructive sleep apnea. (30,31) Nightly episodes of hypoxia, arousals, and swings in intrathoracic pressure due to OSAS may lead to sustained elevation of blood pressure via pathophysiological mechanisms that include chronically elevated sympathetic tone, alterations in baroreceptor function, and cardiovascular remodelling. (32-36)

Sleep related accidents during work or driving a motor vehicle are also reported. A study of 210 patients with untreated sleep apnea reported a threefold increase in the rate of motor vehicle collisions as compared to control subjects. The rates fell to control levels with treatment with continuous positive airway pressure. (37) Lastly, snoring is also a social problem for the partner, and other family members. The patient is often unable to sleep with his/her spouse, and is unable to sleep in hotels or on campings.

Patients with OSAS and an AI <20 have better survival rates than patients with an AI >20 (38).

Diagnosis: history and sleep registration

The main complaint in obstructive sleep apnea is snoring, often accompanied by daytime sleepiness (hypersomnolence), and apneas as noted by the partner. The pathognomonic event - the obstructive apnea- is usually hidden from the patient's consciousness because it occurs while he/she is asleep. The patient is also usually not aware of the loud snoring, irregular breathing patterns, and other physical concomitant events such as restless legs or trashing out in bed. Therefore the patients own history must be supplemented whenever possible, by the observation of those who observe his/her nocturnal behaviour. A variety of

other symptoms can occur as well, such as loss of concentration, poor memory decreased intellectual function, headache, mental alterations, nocturna sweating, nocturia, dry mouth on awakening, sexual impotence and others.

It is however questionable whether the history is reliable enough tc distinguish between simple snoring and obstructive sleep apnea. Is obstructive sleep apnea ruled out if a history is negative for hypersomnolence and the partner does not note apnea? To distinguish between socially unacceptable snoring and OSAS, the rate of apnea and hypopnoea during sleep and the sleep pattern itself needs to be established. The gold standard investigation for sleep apnea is full overnight polysomnography from which the type and severity o sleep apnea may be determined.

The American Sleep Disorders Association has defined four levels o sleep testing. (39)

level 1: standard polysomnography (see below), level 2: unattended overnigh polysomnography. The same items as in the level 1 study are measured, but pe formed in the patient's home. Although on first sight it appears better to recor in as natural circumstances as possible, more data loss occurs in this ambulan setting, due to displaced sensor leads, than in level 1 studies. level 3: limitec sleep studies (respiratory airflow, heart rate and oxymetry only), and level 4 even more limited sleep study: unattended ambulatory recording of only one o two physiological parameters, usually including oxymetry.

The standard complete sleep registration is polysomnography (PSG), a continuous recording, generally through a complete night, but for at least hours. The recording is performed in a sleep laboratory in the presence of a technician. PSG records the sleep architecture (derived from electroencephalogram eye movements and submental electromyogram), respiration (thoracic and abdominal measurement), oxygen saturation, movements of limbs and the intensity of the snoring. (40) Patients with OSAS will demonstrate repeated periods o apnea or hypopnea, concomitant oxygen desaturation of variable severity anc duration and abnormalities in heart rate and rhythm.

The multiple sleep latency test (MSLT) permits an objective assessmen of the patients degree of daytime sleepiness. The patient is monitored during an 8-10 hour period starting the following morning after completing a night o well-defined PSG-monitored sleep. The patient is given 20 minutes opportunities to nap every two hours and is monitored for sleep onset and REM onset in each While MSLT is not necessary to diagnose OSAS, it does permit an objective assessment of daytime sleepiness. The MLTS is especially useful in the diagnosis of other sleep disorders.

Although sleep registration is the best way to distinguish between simple snoring and OSAS, this is a costly and time consuming procedure, and it is for logistic reasons impossible to perform sleep registration in all snorers. Presently, possible alternative ways for differentiating between snoring and OSAS, are raising great interest. The Epworth Sleepiness Scale (ESS) has been developed as a simple and easy to administer questionnaire that provides quantitative measurements of sleep propensity in adults. It was hoped that it would distinguish normals and habitual snorers from those with OSAS. (41) Similar tests have been modified and validated, in other languages, such as a German (Berlin) questionnaire, a Dutch (Rotterdam) questionnaire, and tests in Spanish and Chinese. (42-46) The predictive value of tests as the ESS to distinguish between simple snoring and OSAS has unfortunately proven to be low. (47-49)

ENT examination and topical diagnosis

Sleep registration rules out or establishes the presence of OSAS and it also provides information on the severity of OSAS. It however does not provide insight in possible local causative or general contributing factors. OSAS is caused by obstruction in the upper airway while general factors such as obesity, misuse of alcohol and sedatives, and reduced muscle tonus can play a role as well.

Every patient visiting an otolaryngologist will receive a complete ENT examination. High body mass index (BMI > 30 kg/m2) and larger neck circumference (>44 cm) correlate with more severe OSAS. (50)

An ENT examination of the awake patient in sitting position gives limited information on the exact level(s) of obstruction, because throat muscles relax during sleep. There are several forms of radiographic, endoscopic, and otherwise invasive investigations, which help to identify the location and mechanism of airway collapse.

The Mueller manoeuvre is a test with flexible nasendoscopy. The patient is asked to make an inspiration movement with nose and mouth closed, and the lumen narrowing on oropharyngeal level is visualised. Information on (possible obstruction at lower levels is lacking. The Mueller manoeuvre has been shown to be not very predictable for the success rate of surgery in the form of uvulopalatopharyngoplasty (UPPP). (51-53)

Mallampati *et al* have developed a classification system to predict possible difficulties during intubation depending on tongue size. (54) The system was later modified by Friedman *et al,* including size of the tonsils, to predict the effect of UPPP. In short, the two extremes of this classification system are that in case of a large tongue and absent tonsils the change of success of UPPP is low,

while in case of large tonsils and a relatively small tongue, the change of successful UPPP is much higher. (55)

Lateral cephalometry is widely available, easily performed, but provides limited information about anterior-posterior structures and no information about lateral soft-tissue structures and can not be performed while the patient is sleeping. (56-59)

CT-scanning is widely available, gives accurate information of upper airway cross sectional area and volume, is potentially useful in patients who undergo bony manipulation, but radiation exposure limits ability to perform repeat studies while awake and asleep. (60,61)

MRI gives an accurate assessment of the upper airway cross sectional area and volume, is harmless and has an excellent airway and soft tissue and fat resolution, but is also hard to perform during sleep. (62,63)

Somnofluoroscopy, which has the disadvantage of considerable radiation exposure, has still to be established in larger series as a diagnostic tool. (64)

Rhinosleep, which is based on acoustic reflectometry which consists of measurement of pressure difference (level of obstruction) on oropharyngeal and hypopharyngeal levels by means of a nasogastric pressure tube, might be promising but is still under investigation. (65,66)

Pharyngeal pressure measurement during sleep to detect the level of obstruction is presently under study. The procedure seems promising but also needs further investigation. (67,68)

Sleep(naso)endoscopy during artificially induced sleep has been developed in the hope to approach the natural situation during snoring as good as possible. Although it is clear that artificially induced sleep is not necessarily equal to natural sleep, it appears presently to be the best tool of topical diagnostic work-up for a routine ENT practice. There are two methods to induce the sleeping situa-tion: intravenous administration of propofol, or intravenous administration of Midazolam. (69-74) A downside of the method is that it is time-consuming, relatively costly, complications of the procedure are possible and it is subjective. The method is safe; even in the hands of physicians who are not an anaesthesiologist, when certain strict in- and exclusion criteria are met. (75)

Treatment

There is no lack of would be snoring remedies. A number of ingenious gadgets have been devised which deliver painful or unpleasant stimuli to patients when they snore - as if they could be trained or conditioned (Pavlovian style). (Fig. 2.)

Fig. 2

Unfortunately snoring is purely an involuntary phenomenon, and if these devices work, this is usually because they keep the patient from going to sleep altogether. Until the present day, every few months in the lay press, the newest so-called effective anti-snoring remedy is presented.

In actual fact, heavy snorers and OSAS patients should have an individually tailored treatment advice, after a thorough history has been taken and careful ENT examination has been performed. Additionally, studies in a sleep laboratory (PSG) are essential in adult patients to distinguish between unacceptable snoring and sleep apnea syndrome and if sleep apneu is established, to record its severity. Topical diagnostic work-up is essential when surgery is considered.

For adults with mild or occasional snoring, self-help remedies are worth trying. Patients are advised to exercise to develop good muscle tone and to lose weight. Many patients with obstructive sleep apnea are obese, and weight

reduction is essential in these cases. Unfortunately, it is a clinical reality that it is extremely difficult for these patients to lose weight, and when a lower weight has been reached, to maintain it. Patients should not drink alcohol within 4 hours before retiring. Patients should also avoid tranquillisers, sleeping pills, and antihistamines before bedtime. They should try to sleep sideways rather than on their back. Prevention of the supine position is a well-known treatment in positional obstructive sleep apnea and is also effective in prevention of snoring. Maurer *et al* described good results of a special vest in preventing sleeping in the supine position, (also known as positional therapy). (76) Allergies should be ruled out or treated, especially when the patient complains about nasal obstruction. (21-23) In most cases, however, these conservative measures are useful as adjunctive only to more invasive therapy, either because they are insufficient alone, or because they are difficult to achieve.

In addition to these relatively simpler procedures, various non-surgical surgical and otherwise invasive interventions are available. There is no universally effective panacea. To select the correct form of treatment for the individual patient, with sufficient chance of success, with the least chance of morbidity and complications, with sufficient long-term effect is the biggest challenge in treatment of obstructive sleep apnea.

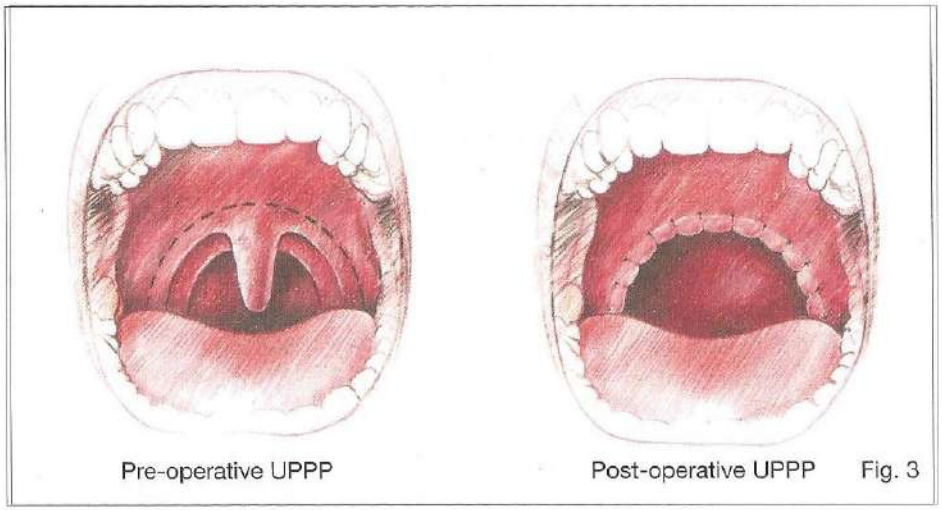
In case of concomitant nasal anatomical pathology nasal surgery can be indicated. (21-23) Of interest is that in some isolated cases, the effect of improved nasal patency after nasal surgery can be impressive, but the effect is not present in all patients. Verse *et al* found that nasal surgery had a limited effect in the treatment of adult patients with obstructive sleep apnea. Nasal surgery especially improved sleep quality and daytime sleepiness independent of the severity of obstructive sleep-related breathing disorders. Overall, these authors found that patients with OSAS and nasal obstruction are "cured" in only about 16 % of cases after nasal surgery alone. (23)

Tracheotomy was the original treatment for patients with far-advanced and life-threatening sleep apnea. Many patients and spouses, who find the appearance, the sound and the care of a tracheotomy to be objectionable, can nowadays find treatment with nasal continuous positive airway pressure (NCPAP). Trachestomy is now only indicated as last refugium, in case NCPAP can not be tolerated and other invasive forms of therapy have failed.

NCPAP is a self-sealing nasal mask through which air under pressure is delivered. NCPAP was introduced in 1981 by Sullivan *et al.* (77) NCPAP therapy works by preventing obstructive apneas and hypopneas by pneumatically splinting the upper airway. (78) The application of NCPAP via a nasal mask has been shown to provide significant amelioration of combined central and obstructive as well as obstructive apnea only with improvement of the nocturnal

oxygenation. NCPAP is regarded as golden standard of treatment especially of severe forms of obstructive sleep apnea. Unfortunately, poor compliance is a major concern, especially in mild to moderate forms (with limited sequelae such as daytime sleepiness) of sleep apnea. (79) Only approximately 50% of OSAS patients can accept long-term use of NCPAP. (80)

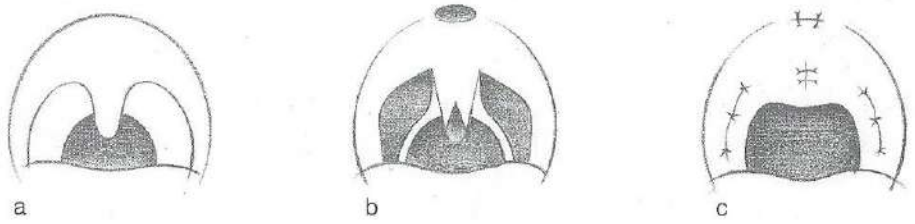
Obstruction on oropharyngeal level can be treated with uvulopalato-pharyngoplasty (UPPP). With UPPP redundant pharyngeal tissue is removed and tightened up and a long floppy uvula and soft palate are shortened. This operation is often combined with tonsillectomy to create as much space as possible in the oropharynx.(Fig.3.)



Pre-operative UPPP Post-operative UPPP Fig. 3

Pharyngeal surgery for snoring began in 1952 in Japan with Ikematsu, when he saw a young woman whose obnoxious snoring had caused her marriage to fail. On examination, he found a redundant posterior pillar of the soft palate with oropharyngeal web formation and an elongated uvula. Removal of this seemingly excessive tissue eliminated the loud snoring. Encouraged to this initial success, he treated more patients whose snoring had seriously disrupted their lives. He reported the results of his surgical treatment of 152 habitual snorers in 1964. (81) His procedure consisted of partial palatectomy - excision of redun-dant posterior pillar mucosa - and partial uvulectomy under local anaesthesia. The treatment was considered successful by 81.6% of his patients.

The technique of his surgery is illustrated in fig.4 (a-c) a) Pre-operative view.



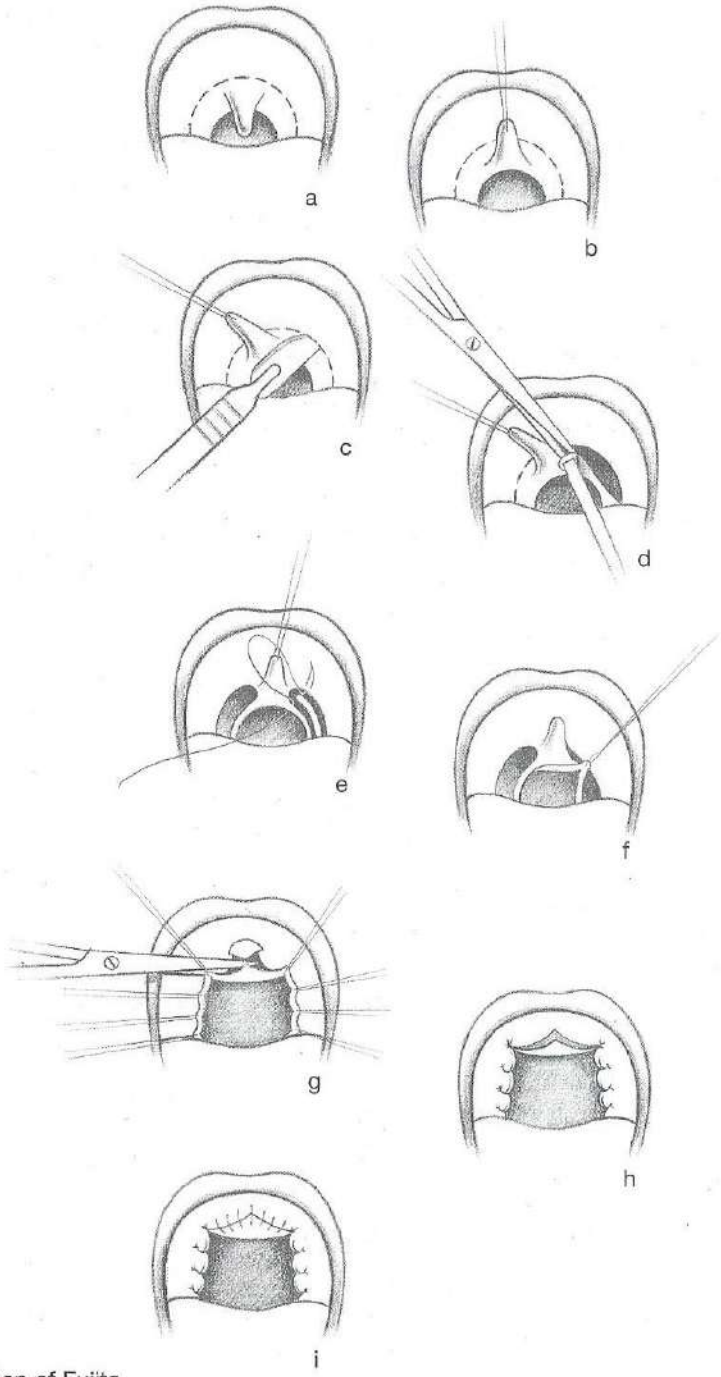
Procedure of Ikematsu

Fig. 4

b) A wedge section is made in the posterior pillar mucosa adjacent to the root of the uvula. The mucosa of the pillar between the palatal arches is then removed and the mucosal edges of the anterior and posterior palatal muscles are approximated. In addition, a small partial resection of mucosa and submucosal tissues from the root of the uvula is performed, with the aim to cause anterior displacement of the uvula. c) Post-operative view.

In 1979 Fujita began to explore the surgical treatment of patients with severe obstructive sleep apnea syndrome, in search of surgical alternatives to tracheotomy. In 1980 he introduced a new operation to correct the anatomic abnormalities of obstructive sleep apnea patients called uvulopalatopharyngoplasty (UPPP). UPPP has been the workhorse of surgical treatment of snoring and OSAS and probably still is the most widely performed surgical procedure for OSAS. (82) The procedure was designed to enlarge the potential airspace in the oropharynx. Fujita has modified the technique since his first publication and this procedure is illustrated in fig.5 (a-i)

The operation is performed under general anaesthesia. a) First inspection of the oropharyngeal structures to determine the dimension of the oropharyngeal inlet is performed. b) A suture is passed through the distal third of the uvula and held by a haemostat attached to the end of the string. When the string is pulled upward, the soft palate is pulled away from the pharyngeal wall, and redundant posterolateral pharyngeal wall mucosa is strechted, expanding the oropharyngeal space. Tonsillectomy is performed if not previously done. c) A mucosal incision is made on the oral side of the soft palate, starting at the midline and extended bilaterally in a curvilinear fashion as far as the base of the tongue. d) The mucosa and submucosal tissues are dissected away between the anterior and posterior arches of the tonsillar fossa. Redundant mucosa is removed from the rim of the posterior pillar, while sparing the underlying musculature. e-f) The palatopharyngeal muscle is grasped with a forceps at its medial third and pulled anterolate



Modification of Fujita

Fig. 5

rally as far as possible before it is sutured into the palatoglossal muscle. g) Interrupted sutures are placed through the muscles between the palatal arches. The uvula is amputated at the base. h-i) A V-shaped incision is made on the palatal mucosa at the base of the uvula, leaving adequate mucosal flap to rotate forward to approximate the mucosal edges of the soft pal-ate on the oral side with sutures. This operation was originally performed on 12 patients with OSAS. In 8 of these 12 patients, nocturnal respiration and sleep architecture improved. In 1985 Fujita published the results of an efficacy study of UPPP for the treatment of OSAS in a series of 66 consecutive patients. (78) Although 76% of these patients reported significant subjective response in daytime sleepiness and 94% of them thought their snoring was much improved, only 50% were considered to have an appreciable reduction in the frequency of their sleep apnea. To classify a patient as a UPPP responder, they required at least a 50% reduction in the apnea index as determined by polysomnographic study 6 weeks after surgery, compared to the preoperative PSG. After retrospective anatomic analyses, it was concluded that UPPP significantly reduced the apnea index only in those patients whose airway obstruction was primarily on oropharyngeal level. If airway obstruction extended in the hypopharynx, UPPP was much less likely to produce a significant reduction in the apnea index.

Roth *et al* investigated the overall response rate to UPPP. (84) From a total of 314 patients, the overall reduction - to 50% of pre-operative AHI - was 49%, with a range of 36% to 85% in the 6 sleep institutions in which they collected their data. Variability of the data was thought to be related to different criteria for selecting patients and to differences in the surgical techniques at the various centers.

Simmons *et al* modified the procedure by Fujita, although it is almost similar both in concept and execution to the technique of UPPP of Fujita. (85) The most outstanding feature is that they do not attempt to recontour the uvula but resect it along with the entire posterior border of the soft palate (Fig 6.).

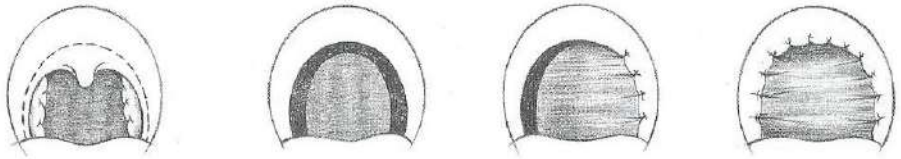


Fig.

Another modification, by Fairbanks, intents to maximise the lateralizatior of the posterior pharyngeal pillars, which would increase the lateral dimensior of the oropharyngeal airway, while sparing midline musculature (91).

Dickson and Blokmanis described the use of 'the dimple point' of the soft palate in order to mark the level of excision and to prevent palate insufficiency postoperatively. (86) Later modifications included a 'Z-plasty' technique to prevent scar contracture of the pharynx and a complete excision of the palatopharyngeal muscle. (87,88)

The modification of Woodson is divided into three stages. The first stage involves a conservative UPPP, the second advances the soft and hard palate, and the third advances the lateral soft palate and closes the wound. (89) Convincing evidence that the results of one of these modifications is superior to the others in terms of result, morbidity and complications is however lacking.

In the eighties of the past century, UPPP was performed as surgical treatment of first choice, and although it was said to be often successful in snoring (roughly 70-80 % success), it was less successful in OSAS patients, with approximately 50 % change of success. At that time generally accepted criteria for success were lacking. Later, criteria for success were developed for treatment of OSAS, being a reduction of the A(H)I of > 50% and reduction of the AHI below 20. (90) Using these criteria in a large meta-analysis it was shown that UPPP was only successful in 41% of OSAS patients, a disappointing low score. (90) Concern has also risen about long term results of UPPP. (90-92)

The procedure can also lead to complications which can be classified into three groups; perioperative, early postoperative, and late postoperative. Perioperatively, airway obstruction or even narrowing of the pharyngeal lumen due to oedema or haemorrhage, which will make the underlying OSAS worse, is a potentially disastrous occurrence. (93-95)

Early postoperative complications in order of frequency are: transient velopharyngeal incompetence usually manifested with wound dehiscence, haemorrhage, wound infection, mild nasal regurgitation and less commonly with hypernasal speech. The procedure is known for its severe pain, and poor dietary intake and its overall morbidity is therefore considerable. (93-95)

Late post-UPPP complications are pharyngeal discomfort, dryness, tightness, postnasal secretions, inability to initiate swallowing, disturbance of taste, and numbness of the tongue.

Because of these reasons, alternative ways of treatment were pursued. Such other forms of surgery and invasive and non-invasive treatment include laser assisted uvulopalatoplasty (LAUP), radiofrequent tissue reduction of the soft palate and base of tongue and oral device therapy.

LAUP was developed by Kamami, in the late 1980s, initially as a treatment for snoring without apnea. (97) The procedure, later modified by Coleman, is performed with the patient sitting in an examination chair in the upright position. (98) After local anaesthetics have been administered along the

posterior palate and the uvula, the procedure is performed with a carbon dioxide laser. The laser is used to make bilateral vertical incisions through and through the palate at the base of the uvula. Subsequently, the uvula is shortened and reshaped. Tonsillectomy is not performed.

The use of oral devices (100-104) (also known as mandibular reposition appliances) and radiofrequent volume reduction of the soft palate (105) also became popular in the nineties of the last century. Oral devices that reposition the mandible, increasing the pharyngeal dimensions, are becoming more common for the treatment of snoring and milder forms of OSAS. Potential complications of oral devices such as temporomandibular joint dysfunction, dry mouth or increased saliva production can necessitate treatment cessation in some patients. A disadvantage of the mandibular reposition appliances is the fact that it implicates life long use since the anatomy is not altered. The efficacy and patient compliance are good in simple snoring and mild to moderate sleep apnea but the effect of oral devices drops with higher apnea hypopnea indices.

Radiofrequent volume reduction of the base of tongue (106-109) is being investigated since the first years of this century, and a variety of other methods such as a tongue retaining thread through the tongue (Repose-system) (110,111), Laser midline glossectomy (112,113), hyoidthyroidpexia (114,115), genioglossal advancement (115,116) maxillomandibular advancement (117-124) alone or in combinations have been analyzed. (125)

Hyoidthyroidpexia is a procedure in which the infrahyoid (strap) muscles are cut, and the tendon of the stylohyoid muscles are cut superiorly. Then the hyoid bone is fixed to the thyroid cartilage with (semi)permanent sutures. The procedure can be indicated in patients with obstruction at base of the tongue level with mild to moderate sleep apnea. (114,115) The procedure can be combined with genioglossal advancement.

The results of LAUP and radiofrequent volume reduction of the soft palate were shown to be similar to that of UPPP. (126-136) Radiofrequent volume reduction seems to have a role in simple snoring and mild sleep apnea or as adjunctive procedure combined with more invasive treatments.

Other researchers were fascinated by the fact that although UPPP is often not successful in obstructive sleep apnea, it can not be disregarded that it still is successful in 41%. How could we distinguish between patients in whom UPPP would probably help and patients in whom other forms of treatment would be better? The path several researchers have followed is combining data from sleep registration and topical diagnosis in order to come to an individually tailored treatment advice. A form of topical diagnosis is crucial in this policy. In case of obstruction on uvulopalatotonsillar level, UPPP remains an option, in case of obstruction on base of tongue level and in case of multilevel obstruction alternative forms op treatment should be offered to the patient. In many cases of multilevel obstruction treatment advice is difficult.

Recent publications in the Netherlands

The present policy with regards to the diagnosis and treatment of snoring and sleep apnea in the Netherlands is to a certain extent based on some recent publications in the Dutch literature.

In 1999, the Dutch Society of Otorhinolaryngology-Head and Neck Surgery published a report on Snoring and Obstructive Sleep Apnea. (137)

In 2000, Boot defended his PhD thesis on pathogenetic aspects and treatment of OSAS. Important in the thesis was that the results of UPPP in these (not via sleep endoscopy selected) patients were slightly less succesful as compared to historical controls in the literature, and that the results worsened with long-term follow-up. (138)

In 2001, the Kwaliteitsinstituut voor de Gezondheidszorg CBO (Quality Institute for Health Care) published a Consensus Document on Diagnosis and Treatment of Obstructive Sleep Apnea Syndrome (in adults), in which all aspects of snoring and OSAS where comprehensively reviewed for the first time. (139)

In 2003, a Caput Selectum appeared in the Netherlands Journal of Medicine (NTVG) on Treatment of sleep apnea in adults. In this paper, it was stressed that treatment with oral devices or NCPAP is to be preferred and that surgical treatment should be reserved for refusal or non-acceptance of oral device and NCPAP. (140)

In a reaction on this paper, we underlined that results of surgery can be improved by better patient selection and that ideally an individually tailored treatment advice is important. (141).

Outline of the thesis

In **Chapter two** of the thesis, our experiences and findings with sleep registration are discussed. Our sleep registration findings were compared with key complaints in the history; snoring, hypersomnolence and apnea as reported by the partner. We were interested to see whether a positive history of hypersomnolence and apnea would implicate sleep apnea, and vice versa, if a negative history for hypersomnolence and apneu as reported by the partner, would mean that sleep apnea is ruled out.

In **Chapter three**, we report our findings with topical diagnosis in the form of sleep endoscopy in the same patients. What is the most often occurring

level of obstruction, how frequent is unilevel obstruction and on which level and how frequent is multilevel obstruction? Our protocol, inclusion and exclusion criteria, results and complications are presented here.

In **Chapter four**, we discuss our experience with the Rhinosleep flextube, a possible alternative way of topical diagnosis, in the form of a feasibility study. If this method, performed during sleep registration, would be feasible, this could become a viable alternative, or addition, to sleep endoscopy.

Based on the results presented in chapters 2 and 3, an individual tailored treatment advice was given to the patient. As a rule, several treatment modalities were discussed with patient and partner. Treatment options included general treatment advices such as weight reduction, positional therapy, avoidance respectively reduction of alcohol, sedatives and narcotics, and locally, various forms of surgical and other invasive and non invasive interventions such as radiofrequent ablation of the soft palate, inferior turbinates and base of tongue, nasal and paranasal sinus surgery, UPPP with and without tonsillectomy, oral appliances, hyoidthyroidpexia, NCPAP and combinations. In case of obstruction on uvulopalatotonsillar level and socially unacceptable snoring, and mild to moderate sleep apnea, the choice was between UPPP -in case of large tonsils, long uvula, redundant pharyngeal walls, relatively higher AHI, mild to moderate sleep apnea-, and radiofrequent ablation -in case of absent tonsils, relatively short uvula-, or oral device. In case of obstruction on base of tongue level, the choice was between oral device, radiofrequent ablation of the base of tongue -socially unacceptable snoring, and mild to moderate sleep apnea-, hyoidthyroid-pexia -moderate to severe sleep apnea-, or NCPAP -severe sleep apnea-, and depending on the patient's preference and the AHI level. In case of decreased nasal patency, this was usually corrected first, medically, surgically or both. Surgical treatment for nasal or nasopharyngeal obstruction included septoplasty, radiof-requent ablation or partial resection of the inferior turbinates adenoidectomy and functional endoscopic sinus surgery (FESS).

In the studyperiod it was policy in case of multilevel obstruction (uvulo-palatotonsillar and base of tongue level), to start with UPPP, and in case of UPPP failure, to offer oral device therapy, hyoidthyroidpexia, or NCPAP respectively as salvage therapy. Based on this policy, a considerable number of the total number of patients was offered UPPP as one of the treatment modalities, and a major part of these patients agreed to undergo UPPP. Of all the various forms of surgical and otherwise invasive interventions, we focus in this thesis on the results of UPPP only since this was by far the largest group of surgical treatments. In **Chapter five** are the results of UPPP based on this policy reported.

In some cases UPPP will not help, and unfortunately, the results of UPPP can even be negative, making the situation worse. This is a relatively new and underreported item in the literature. Negative results occurred in our, with sleep endoscopy selected, patients as well. In **Chapter six**, we look at possible predictive parameters of negative outcome of UPPP.

This thesis is completed by a summary, conclusions, and a look at future developments.

References

1. Boulware MH. Snoring, new answers to an old problem. Rockaway, NJ: American Faculty Press, 1974.
2. Kryger MH. Sleep apnea: from the needles of Dionysius to continuous positive airway pressure. Arch Inter Med 1983; 143; 2301-2303.
3. Cited in: Loadsman JA, Hillman DR. Anaesthesia and sleep apnoea. Br J Anaesthesia 2001; 86(2): 254-266.
4. Dickens Ch. The posthumous papers of the Pickwick Club 1837.
5. Gastaut H, Tassinari CA, Duron. Polygraphic study of episodic diurnal and noctural hypnic and respiratory manifestations of the Pickwick syndrome. Brain Res 1966; 1: 167-186.
6. Lugaresi E. Hypersomnia with periodic breathing. Symposium Rimini, Italy 1972: 967-1292.
7. Kryger M, Roth T, Dement WC, Eds. Principles and practice of sleep medicine. 2nd ed. Philadelphia: WB Saunders 1994; pp 667-67.
8. Chaudhary BA, Speir WA. Sleep apnea syndromes. South Med J 1982; 75: 39-45.
9. AASM taskforce report: sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep 1999; 22: 667-689.
10. Tsai WH, Flemons WW, Whitelaw WA, Remmers JE. A comparison of apneahypopnea indices derived from different definitions of hypopnea. Am J Respir Crit Care Med 1999; 159: 43-48.
11. American Sleep Disorders Associations (1997) standards of practice: The indications for polysomnography and related procedures. Sleep 20; 6: 423-487.
12. Lugaresi E, Mondini S, Zucconi M, Montagna P, Cirignotta F. Staging of heavy snorers disease. A proposal. Bull Eur Physiopathol Resp 1983; 19: 590-594.
13. Lugaresi E, Cirignotta F, Coccagna G, Piana C. Some epidemiological data on snoring and cardiocirculatory disturbances. Sleep 1980; 3: 221-224.
14. Woodhead CJ, Davies JE, Allen MB. Obstructive sleep apnea in adults presenting with snoring. Clin Otolaryngol 1991; 16: 401-405.
15. Knuistingh Neven A, Middelkoop HAM, Kemp B, Kamphuisen HAC, Springer MP. The prevalence of clinical significant sleep apnea syndrome in the Netherlands. Thorax 1998; 53 (80: 638-642.
16. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea. Am J Respir Crit Care Med 2002; 165: 1217-1239.
17. Ancoli-Israel S, Klauber M, Strepnowsky C, Estline E, Chinn A, Fell R. Sleep disordered breathing in African-American eldery. Am J Respir Crit Care Med 1995; 152: 1946-1949.
18. Suratt PM, Dee P, Atkison RL, Armstrong P, Wilhoit SC. Fluoroscopic and computed tomographic features of the pharyngeal airway in obstructive sleep apnea. Am Rev Respir Dis 1983; 127: 487-492.
19. Haponik EF, Smith PL, Bohiman ME, Allen RP, Goldman SM, Bleecker ER. Computerized tomography in obstructive sleep apnea. Am Rev Respir Dis 1983; 127: 221-226.
20. Fairbanks DNF. Snoring; surgical vs. nonsurgical management. Laryngo-scope 1984; 94: 1188-1192.
21. Ellis PD, Harries ML, Ffowcs Williams JE, Shneerson JM. The relieve of snoring by nasal surgery. Clin Otolaryngol 1992; 17: 525-527.
22. Fairbanks DNF. Effect of nasal surgery on snoring. South Med J 1985; 78: 268-270.
23. Verse T, Maurer JT, Pirsig W. Effect of nasal surgery on sleep-related breathing disorders. Laryngoscope 2002; 112: 64-68.
24. Koskenovuo M, Partinen M, Sarna S, *et al.* Snoring as a risk factor for hypertension and angina pectoris. Lancet 1985; 23: 893-896.
25. Koskenvuo M, Kaprio J, Letakivi T, et al. Snoring as a risk factor for ischaemic heart disease and stroke in men. BMJ Clin Res Ed 1987; 294: 16-19.
26. Koskenvuo M, Partinen M, Kaprio J, *et al.* Snoring and cardiovascular risk factors. Ann Med 1994; 26: 371-376.
27. Palomaki H, Partinen M, Juvela S, Kaste M. Snoring as a risk factor for sleep-related brain infarction. Stroke 1989; 20: 1311-1315.
28. Hung J, Whitford EG, Parsons RW, Hillman DR. Association of sleep apnoea with myocardial infarction in men. Lancet 1990; 336: 261-264.
29. Montplaisir J, Bedard MA, Richer F, Rouleau I. Neurobehavioral manifestations in obstructive sleep apnea syndrome before and after treatment with continuous positive airway pressure. Sleep 1992; 15: S17-S19.
30. Guilleminault C, Tilkian A, *et al.* The sleep apnea syndrome. Ann Rev Med 1976; 27: 465-484.
31. Lavie P, Yoffe N, *et al.* The relationship between the severity of the sleep apnea syndrome and 24-hours blood pressure values in patients with obstructive sleep apnea. Chest 1993; 103: 717-723.
32. Weiss JW, Remsburg S, Garpestad E, Ringler J, Sparrow D, Parker JA. Hemodynamic consequences of obstructive sleep apnea. Sleep 1996; 19: 388-397.

33. Dempsey JA. Sleep apnea cauases daytime hypertension. J Clin Invest 1997; 99:1-2.
34. Fletcher EC, Obstructive sleep apnea and cardiovascular death: cause-effect? Monaldi Arch Chest Dis 1995; 50: 340-341.
35. Fletcher EC. Hypertension in patients with sleep apnea: a combined effect? Thorax 2000; 55: 726-728.
36. Hedner JA, Wilcox I, Sullivan CE. Speculations on the interaction between vascular disease and obstructive sleep apnea. In: Saunders NA, Sullivan CE, editors. Sleep and breathing, 2nd ed. New York: Marcel Dekker;1994. p. 823-846.
37. George CF. Reduction in motor vehicle collisions following treatment of sleep apnoea with nasal CPAP. Thorax 2001; 56: 508-512.
38. HE J, Kryger MH. Mortality and apneu index in obstructive sleep apnea. Chest 1988; 94: 9-14.
39. Standards of Practice Committee of the American Sleep Disorders Association. Practice parameters for the indications of polysomnography and related procedures. Sleep 1997;20(6): 406-422.
40. Fairbanks DNF, Fujita S. Snoring and obstructive sleep apnea. 2nd Ed, 1994.
41. Johns M. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991; 14: 540-545.
42. Bloch KE, Schoch OD, Zhang JN, Russi EW. German version of the Epworth sleepiness scale. Respiration 1999; 66: 440-447.
43. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Int Med 1999; 131: 485-491.
44. Chen N-H, Johns MW, Li H-Y, Hu C-C, Liang S-C et al. Validation of a Chinese version of the Epworth sleepiness scale. Quality of life research 2002; 11: 817-821.
45. Knippenberg FCE van, Passchier J, Heysteck D, Shackleton D, Schmitz P, Poublon RML, Meche F van der. The Rotterdam daytime sleepiness scale: a new daytime sleepiness scale. Psychological reports 1995; 76: 83-87.
46. Chiner E, Arriero JM, Signes-Costa J, Marco J, Fuentes I. Validation of the Spanish version of the Epworth sleepiness scale in patients with a sleep apnea syndrome. Arch Bronconeumol 1999: 35: 422-427.
47. Osman EZ, Osborne J, Hill PD, Lee BWV. The Epworth Sleepiness Scale: can it be used for sleep apnoea screening among snorers? Clin Otolaryngol 1999; 24: 239-241.
48. Chervin RD, Aldrich MS. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnoea. Neurology 1999; 52: 125-131.
49. Kingshott RN, Sime PJ, Engleman HM, Douglas NJ. Self-assessment of daytime sleepiness: patient versus partner. Thorax 1995; 50: 994-5.
50. Martimore IL, Marshal I, et al. Neck and total body fat deposition in nono-bese and obese patients with sleep apnea compared with that in control stud-ies. Am J Respir Crit Care Med 1998;157: 280-283.
51. Sher AE, Trophy MJ, Sphrintzen RJ, Spielman AJ, Burack B, McGregor PA. Predictive value of Mueller Manoeuvre in selection of patients for uvulopalatopharyngoplasty. Laryngoscope 1985; 95: 1483-1487.
52. Boot H, Poublon RM, van Wegen R, Bogaard JM, Schmitz PI, Ginai AZ, van der Meche FG. Uvulopalatopharyngoplasty for the obstructive sleep apnoea syndrome: value of polysomnography, Mueller manoeuvre and cephalometry in predicting surgical outcome. Clin Otolaryngol 1997; 22: 504-510.
53. Pringle MB, Croft CB. A comparison of sleep endoscopy and the Mueller manoeuvre. Clin Otolaryngol 1991; 16: 559-562.
54. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J 1985; 32(4): 429-434.
55. Friedman M, Tayeri H, LaRosa M, et al. Clinical predictors of obstructive sleep apnea. Laryngoscope 1999; 109: 1901-1909.
56. Deberry-Borowiecki B, Kukwa A, Blanks RH. Cephalometric analysis for diagnosis and treatment of obstructive sleep apnoea. Laryngoscope 1988; 98(2): 226-234.
57. Mochizuki T, Okamoto M, Sano H, Naganuma H. Cephalometric analysis in patients with obstructive sleep apnoea syndrome. Acta Otolaryngol 1996; 524: 64-72.
58. Partinen M, Guilleminault C, Quera-Salva MA, Jamieson A. Obstructive sleep apnoea and cephalometric roentgenograms. The role of anatomic upper airway abnormalities in the definition of abnormal breathing during sleep. Chest 1988; 93(6): 1199-1205.
59. Riley R, Guilleminault C, Herran J, Powell N. Cephalometric analysis and flow loops in obstructive sleep apnea patients. Sleep 1983; 6(4): 303-311.
60. Stein MG, Gamsu G, de Geer G, Golden JA, Crumley RL, Webb WR. Cine CT in obstructive sleep apnoea. AJR 1987; 148 (6): 1069-1074.

61. Ryan CF, Lowe AA, Li D, Fleetham JA (1991) Three-dimensional upper airway computed tomography in obstructive sleep apnoea. Am Rev Respir Dis 1991; 144: 428-432.
62. Suto Y, Matsuo T, Kato T, Hori I, Inoue Y, Ogawaw S, Suzuki T, Yamada M, Otha Y. Evaluation of the pharyngeal airway in patients with sleep apnoea: Value of ultrafast MR imaging. AJR 1993; 160(2): 311-314
63. Hasegawa K, Nishimura T, Mikio Y, Natsuki M, Nobuhiro S, Kiouchi I. Diagnosis by dynamic MRI in sleep disordered breathing. Acta Otolaryngol 1996; 523: 235-247.
64. Katsantonis GP, Walsh JK. Somnofluoroscopy: its role in the selection of candidates for uvulopalatopharyngoplasty. Otolaryngol-Head Neck Surg 1986; 94(1): 56-60.
65. Faber CE, Grymer LF, Norregaard O, Hilberg O. Flextube reflectometry for localisation of upper airway narrowing- a preliminary study in models and awake subjects. Respir Med 2001; 95: 631-633.
66. Faber CE, Hilberg O, Jensen FT, Norregaard O, Grymer L. Flextube reflectometry for determination of sites of upper airway narrowing in sleeping obstructive sleep apnoea patients. Respir Med 2001; 95: 639-648.
67. Rollheim J, Osnes T, Miljeteig H. The sites of obstruction in OSA, identified by continuous measurements of airway pressure and flow during sleep: ambulatory versus in-hospital recordings. Clin Otolaryngol 1999; 24: 502-506.
68. Verse T, Pirsig W. Pharyngeal pressure measurements in topodiagnosis of obstructive sleep apnea. HNO 1997; 45(11): 898-904.
69. Croft CB, Pringle M. Sleep endoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol 1991; 16: 504-509.
70. Pringle MB, Croft CB. A grading system for patients with obstructive sleep apnoea – based on sleep endoscopy. Clin Otolaryngol 1993; 18: 480-484.
71. Quinn SJ, Daly N, Ellis PD. Observation of the mechanism of snoring using sleep endoscopy. Clin Otolaryngol 1995; 20(4): 360-364.
72. Sadaoka T, Kakitsuba N, Fujiwara Y, Kanai R, Takahashi H. The value of sleep endoscopy in the evaluation of patients with suspected sleep-related breathing disorders. Clin Otolaryngol 1996; 21(6): 485-489.
73. Camilleri AE, Ramamrthy L, Jones PH. Sleep endoscopy: what benefit to the management of snorers? J Laryngol Otol 1995; 109(12): 1163-1165.
74. Marais J. The value of sedation endoscopy: a comparison between snoring and non-snoring patients. Clin Otolaryngol 1998; 23: 74-76.
75. Knape JTA, Everdingen JJE. Guideline for administration of sedatives and analgesics by physicians who are not anaesthesiologists. National Organisation for quality assurance in hospitals. Neth J Med 1999; 143(21): 1098-1102.
76. Maurer JT, Stuck BA, Hein G, Verse T, Hormann K. Treatment of obstructive sleep apnea with a new vest preventing the supine position. Dtsch Med Wochenschr 2003; 128: 71-75.
77. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnea by continuous positive airway pressure applied through the nares. Lancet 1981; 1: 862-865.
78. Popper RA, Ledinger MJ, Williams AJ. Endoscopic observations of the pharyngeal airway during treatment of obstructive sleep apnea with nasal continuous positive airway pressure – a pneumatic splint. West J Med 1986; 144; 83-85.
79. Grunstein RR. Sleep-related breathing disorders. 5. Nasal continuous positive airway pressure treatment for obstructive sleep apnoea. Thorax 1995; 50: 1106-1113.
80. Sanders MH. Nasal CPAP effects on patterns of sleep apnea. Chest 1984; 86: 839-844.
81. Ikematsu T. Study of snoring. 4th report. Therapy [in Japanese]. J Jpn Otol Rhinol Laryngol Soc 1964; 64: 434-435.
82. Fujita S, Conway W, Zorick F, Roth T. Surgical correction of anatomic abnormalities in OSAS: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 1981; 89: 923-934.
83. Fujita S, Conway WA, Sicklesteel JM, Wiitg RM, Zorick FJ, Roehrs TA, Roth T. Evaluation of the effectiveness of uvulopalatopharyngoplasty. Laryngoscope 1985; 95: 70-74.
84. Roth T. UPPP update. Presented at the annual meeting of American College of Chest Physicians, San Antonio, Texas, October 1984.
85. Simmons FB, Guilleminault C, Silvestri R. Snoring and some obstructive sleep apnea can be cured by oropharyngeal surgery: palatopharyngoplasty. Arch Otolaryngol 1983;109: 503-507.
86. Dickson R, Blokmanis A. Treatment of obstructive sleep apnea by uvulopalatopharyngoplasty. Laryngoscope 1987; 97: 1054-1058.
87. Koopman CF, Moran WB. Surgical management of obstructive sleep apnea. Otolaryngol Clin North Am 1990; 23: 787-808.
88. O`Leary MJ, Millman RP. Technical modification of uvulopalatopharyngoplasty. The role of the palatopharyngeus. Laryngoscope 1991; 101: 1332-1335.

89. Woodson BT, Toohill RJ. Transpalatal advancement pharyngoplasty for obstructive sleep apnea. Laryngoscope 1992; 103: 269-276.
90. Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 1996; 19: 156-177.
91. Boot H, van Wegen R, Poublon RM, Bogaard JM, Schmitz PI, van der Meche FG. Long term results of uvulopalatopharyngoplasty for obstructive sleep apnea syndrome. Laryngoscope 2000; 110: 469-475.
92. Janson C, Gislason T, Bengtsson H, Eriksson G, Lindberg E, Lindho CE. Hultcrantz E, Hetta J, Boman G. Long term follow-up of patients with obstructive sleep apnea treated with uvulopalatopharyngoplasty. Arch Oto-laryngol Head Neck Surg 1997; 123: 257-262.
93. Fairbanks DN. UPPP complications and avoidance strategies. Otolaryngol Head Neck Surg 1990; 102: 239-245.
94. Moran WB. Uvulopalatopharyngoplasty: variations. In: Fairbanks DN, ed. Snoring and obstructive sleep apnea. New York: Raven Press, 1987; 156-160.
95. Telian S, Fleisher G, Marsh R, et al. Effects of antibiotic use on recovery after tonsillectomy in children: a controlled study. Otolaryngol Head Neck Surg [suppl]; 1984: 32.
96. Manni JJ, Wouter HJ, Folgering HT. Sleep apnea syndrome, snoring and uvulopalatopharyngoplasty. [article in German] Laryngol Rhino Otol 1986; 65: 566-569.
97. Kamami Y-V. Laser CO2 for snoring: preliminary results. Acta Otolaryngol Belg 1990; 44: 451-456.
98. Coleman JA. Laser-assisted uvulopalatoplasty: long term results with a treatment fot snoring. Eur Nose throat J 1988; 77: 22-24, 26-29, 32-34.
99. Krespi YP, Kacker A. Laser-assisted uvulopalatoplasty revisited. Otolaryngol Clin North Am 2003;36: 495-500.
100. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perrez-Guera F, Menn S. Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 1995; 18(6): 501-510.
101. Lindman R, Bondermark. A review of oral devices in the treatment of habitual snoring and obstructive sleep apnea. Swed Dent J 2001; 25: 39-51.
102. Mohsenin N, Mostofi MT, Mohsenin V. the role of oral appliances in treating obstructive sleep apnea. J Am Dent Assoc 2003; 134(4): 442-449.
103. Wade PS. Oral appliance therapy for snoring and sleep apnea: preliminary report of 86 patients fitted with an anterior mandibular positioning device, the Silencer. J Otolaryngol 2003; 32: 110-113.

104. Prathibha BN, Jagger RG, Saunders M, Smith AP. Use of a mandibular advancement device in obstructive sleep apnoea. J Oral Rehabil 2003; 30(5): 507-509.
105. Powell N, Riley RW, Troell R, Li K, Guilleminault C. Radiofrequency volumetric tissue reduction of the palate in subjects with sleep disordered breathing. Chest 1998; 113: 1163-1174.
106. Powell N, Riley RW, Guilleminault C. Radiofrequency tongue base reduc-tion in sleep disordered breathing. Otolaryngol Head Neck Surg 1999; 120: 656-664.
107. Woodson T, Nelson L, Mickelson S, Huntley T, Sher A. A Multi-institutional study of radiofrequent volumetric tissue reduction for OSAS. Otolaryngol Head Neck Surg 2001;125: 303-311.
108. Stuck BA, Maurer J, Hormann K. Tongue base reduction with radiofrequency tissue ablation: preliminary results after two treatment sessions. Sleep Breath 2000;4(4): 155-162.
109. Li KK, Powell NB, Riley RW, Guilleminault C. Temperature-controlled radiofrequency tongue base reduction for sleep-disordered breathing: long term outcomes. Otolaryngol Head Neck Surg 2002; 127(3): 230-234.
110. Woodson BT. A tongue suspension suture for obstructive sleep apnea and snorers. Otolaryngol Head Neck Surg 2001; 124(3); 297-303.
111. DeRowe A, Gunther E, Fibbi A, Lehtimaki K, Vahatalo K, Maurer J, Ophir D. Tongue-base suspension with a soft tissue-to-bone anchor for obstructive sleep apnea: preliminary clinical results of a new minimally invasive technique. Otolaryngol Head Neck Surg 2000; 122(1): 100-103.
112. Yonekura A, Kawakatsu K, Suzuki K, Nishimura T. Laser midline glossectomy and lingual tonsillectomy as treatments for sleep apnea syn-drome. Acta Otolaryngol Suppl 2003; 550: 56-58.
113. Mickelson S, Rosenthal L. Midline glossectomy and epiglottidectomy for obstructive sleep apnea syndrome. Laryngoscope 1997; 107; 614-619.
114. Hormann K, Hirth, Erhardt T, Maurer JT, Verse T. Modified hyoid suspension for therapy of sleep related breathing disorders; operative technique and complications. Laryngorhinootology 2001; 80: 517-521.
115. Neruntarat. Genioglossus advancement and hyoid myotomy under local anaesthesia. Otolaryngol Head Neck Surg 2003; 129(1): 85-91.
116. Li KK, Riley RW, Powell NB, Troell RJ. Obstructive sleep apnea surgery: genioglossus advancement revisited. J Oral Maxillofac Surg 2001;58(10): 1181-1184.
117. Costello BJ, Osnick JC. The role of maxillofacial osteotomies in the treatment of obstructive sleep apnea. Curr Opin Otolaryngol Head Neck Surg 2003; 11(40): 267-374.

118. Goh YH, Lim KA. Modified maxillomandibular advancement for the treatment of obstructive sleep apnea: a preliminary report. Laryngoscope 2003;1139(9): 1155-1582.
119. Li KK, Riley RW, Powell NB, Guilleminault C. Maxillomandibular advancement for persistent obstructive sleep apnea phase I surgery in patients without maxillomandibular deficiency. Laryngoscope 2000; 100: 1684-1688.
120. Li KK, Troell RJ, Riley RW, Powell NB, Koester U, Guilleminault C. Uvulopalatoplasty, maxillomandibular advancement and the velopharynx. Laryngoscope 2001; 111: 1075-1078.
121. Li KK, Powell NB, Riley RW, Troell RJ, Guilleminault C. Long term results of maxillomandibular advancement surgery. Sleep Breath 2000; 4(3): 137-140.
122. Bettega G, Pepin JL, Veale D, Deschaux, Raphael B, Levy P. Obstructive sleep apnea syndrome. Fifty-one consecutive patients treated with maxillofacial surgery. Am J Respir Crit Care Med 2000:162: 641-649.
123. Hendler BH, Costello BJ, Silversein K, Yen D, and Goldberg A. A protocol for uvulopalatoplasty, mortised genioplasty, and maxillomandibular advancement in patients with obstructive sleep apnea: an analysis of 40 cases. Oral Maxillofac Surg 2001;59(8): 892-897.
124. Prinsell JR. Maxillomandibular advancement surgery for obstructive sleep apnea syndrome. J Am Dent Assoc 2002; 133(11): 1489-1497.
125. Friedman M, Ibrahim H, Lee G, Joseph NJ. Combined uvulopalatopharyngoplasty and radiofrequency tongue base reduction for treatment of obstruc-tive sleep apnea/hypopnea syndrome. Otolaryngol Head Neck Surg 2003:129(6): 611-21.
126. Kyrmizakis DE, Chimona TS, Papdakis CE, Bizakis JG, GA, Schiza A, Siafakas NM, Helidonis ES. Laser-assisted uvulopalatoplasty for the treatment of snoring and mild obstructive sleep apnea syndrome. J Otolaryngol 2003; 32(3): 174-179.
127. Kern RC, Kutler DI, Reid KJ, Conley DB, Herzon GD, Zee P. Laser-assisted uvulopalatoplasty for the management of obstructive sleep apnea syndrome. Laryngoscope 2003; 113: 1175-1181.
128. Kern RC. LAUP reconsidered. Arch Otolaryngol Head Neck Surg 2003; 129 (4): 494-495.
129. Ferguson KA, Heighway K, Ruvby RR. A randomized trial of laser-assisted uvulopalatoplasty in the treatment of mild obstructive sleep apnea. Am J Respir Crit Care Med 2003:167: 15-19.
130. Fischer Y, Khan M, Mann WJ. Multilevel temperature-controlled radiofrequency therapy of soft palate, of tongue and tonsils in adults with obstructive sleep apnea. Laryngoscope 2003; 113(10): 1786-1791.
131. Tatla T, Sandhu G, Croft CB, Kotecha B. Celon (®). Radiofrequency thermo-ablative palatoplasty for snoring – a pilot study. J Laryngol Otol 2003 117(10): 801-806.
132. Hamans E, Boudewyns A, van den Heyning P. Radiofrequency volumetric reduction of the palate in patients with sleep related breathing disorders. Acta Otorhinolaryngol Belg 2002; 56(2): 183-187.
133. Woodson BT, Steward DL, Waever E, Javaheri S. A randomised trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 2003; 128(6): 848-861.
134. Siad B, Strome M. Long-term results of radiofrequency volumetric tissue reduction of the palate for snoring. Ann Otol Rhinol Laryngol 2003; 112(3): 276-279.
135. Blumen MB, Dahan S, Fleury B, Hauser-Hauw C, Chabolle F. Radiofrequency ablation for the treatment of mild to moderate obstructive sleep apnea. Laryngoscope 2002; 112(11): 2086-2092.
136. Li KK, Powell NB, Riley RW, Troell RJ, Guilleminault C. Radiofrequency volumetric reduction of the palate: an extended follow-up study. Otolaryngol Head Neck Surg 200; 1222(3): 410-414.
137. Adriaansen FCPM. Snurken - Obstructief Slaap-apneu. Report for the Dutch Society of Otorhinolaryngology – Head and Neck Surgery 1999 pp 1-110.
138. Boot H. Obstructive sleep apnea syndrome. Pathogenetic aspects and treatment. 2000, Rotterdam, PhD thesis.
139. De Groen JHM, Keimpema ARJ van, Meulen FW van der (eds.) Diagnosis and treatment of obstructive sleep apnea syndrome (OSAS) in adults.Van Zuiden Communications BV, Alphen aan de Rijn, the Netherlands, 2001, pp 1-204.
140. Hoekema A, Wijkstra PJ, Buiter CT, van der Hoeven JH, Meinesz AF, de Bont LG. Behandeling van het obstructief slaapapneusyndroom bij volwassenen. Ned Tijdschr Geneeskd 2003; 147: 2407-2412.
141. Vries N de, Herder C den, Hessel NS. Behandeling van het obstructief slaapapneusyndroom bij volwassenen. Ned Tijdschr Geneeskd 2004; 148: 250-251.

Chapter 2

Diagnostic work up of socially unacceptable snoring. History or sleep registration

Natascha S Hessel MD (1),
Martin Laman MD (2),
Vincent CPJ van Ammers (2),
Hans van Duijn MD PhD (2),
Nico de Vries, MD PhD (1)

(1) Department of Otorhinolaryngology/
Head and Neck Surgery, Saint Lucas Andreas
Hospital, Amsterdam, The Netherlands
NS Hessel, resident,
N de Vries, otorhinolaryngologist

(2) Department of Clinical Neurophysiology, Saint Lucas
Andreas Hospital, Amsterdam, The Netherlands
DM Laman and H van Duijn, neurophysiologists,
VCJP van Ammers

Eur Arch Otorhinolaryngol 2002 Mar;259(3):154-7

Abstract

Should all patients with socially unacceptable snoring (SUS) have polysomnography or is history taking sufficient to identify the presence of obstructive sleep apnoea syndrome (OSAS)?

Three hundred and eighty consecutive patients with SUS who underwent sleep registration, were evaluated retrospectively to determine the predictive value of a history of apnoea or excessive daytime somnolence (hypersomnia). Of the analysed patients 54 % had OSAS, defined as an apnoea / hypopnoea index (AHI) of >15. This is higher than previously reported in the literature (46.7%). Complaints of (incidental) apnoea were reported by 337 (89 %) of the patients, with a sensitivity of 0.92, and a specificity of 0.13. The predictive value-as related to the gold standard -sleep registration- for a negative test and for a positive test for OSAS is low (0.56 and 0.59, respectively). Hypersomnia was reported by 280 (74%) of the patients, with a sensitivity of 0.29 and specificity of 0.72. The predictive value for a negative test and a positive test for OSAS is low again, 0.45 and 0.56 respectively.

These data confirm that apnoea and hypersomnia in the history do not have a reliable predictive value for an obstructive sleep apnoea syndrome. We conclude that in all patients with SUS, sleep registration is indicated to rule out or confirm the presence of OSAS.

Key words

Apnoea • Hypersomnia • Obstructive sleep apnoea syndrome • Sleep registration • Snoring

Introduction

Snoring is the cardinal symptom of the obstructive sleep apnoea-hypopnoea syndrome (OSAS) which consists of nocturnal snoring interrupted by recurrent obstructive apnoeas and hypopnoeas and often daytime somnolence as a consequence of sleep fragmentation. While snoring is prevalent in up to 24 % [1-6] of men and 14 % [4-6] of women, it is estimated that OSAS affects only 1.1 % of the Dutch population [7]. In another study, OSAS was found in 46.7 % of socially unacceptable snoring (SUS) patients after sleep registration [8]. It is important to differentiate between SUS and OSAS because of the long-term complications of OSAS such as hypertension, right sided heart failure, cardiac arrythmia, sudden death, stroke and depression [4-6,9-11]. General and local factors both play a role in the aetiology of snoring and OSAS. The most general common factors are obesity, alcohol abuse, use of sleep medication and sedatives [12-15].

Analysis starts with history taking and a general ear, nose and throat (ENT) examination. Specific OSAS related examinations such as the Mueller manoeuvre [16-18] and sleep endoscopy [18-21] to determine the site of obstruction are used as well. In addition, the Epworth Sleepiness Scale (ESS), a questionnaire regarding hypersomnia [22-24] and/or the nocturnal sleep registration [25-27] are used to identify the presence of OSAS. The present discussion focuses on the reliability, cost effectiveness, user-friendliness and feasibility of the diagnostic tools used. The predictive value of the ESS has proven to be low [23,28,29].

It seems that there is a spectrum of snoring varying from minor snoring to severe OSAS. Differentiating between snoring and OSAS by means of good diagnostic tools is also of importance since snoring and different levels of OSAS require different treatment.

Since 1995, our diagnostic work-up for all patients with SUS consists of sleep registration as well as sleep endoscopy. The purpose of this part of the study is to evaluate the feasibility, value and results of sleep registration.

Materials and Methods

All patients with SUS seen between February 1995 and April 1999 were included in this study. In all patients, the results of the overnight polysomnography were compared with complaints of apnoea and hypersomnia as noted prospectively in the medical files, by means of sensitivity analysis. In our population a complete ESS was not registered, but hypersomnia was noted positive or negative in the patient medical charts. The medical charts which contained information about both symptoms were analysed in two different ways. Firstly, patients with two positive symptoms were compared with the other three groups. Secondly, patients with two negative symptoms were compared with the other three groups.

For sleep registration we used a CNS-Sleep I/T-8 recorder, which records the sleep architecture (derived from electroencephalogram, eye movements and submental electromyogram), respiration (thoracic and abdominal measurement), oxygen saturation, movements of limbs and the intensity of the snoring. An apnoea / hypopnoea index (AH Index) of more than 15 apnoeas per hour established OSAS and an AHI of more than 30 was graded as a severe OSAS [30]. The body mass index (BMI) was calculated in all patients. A BMI of more than 25 was regarded as obesity [31]. The relation between BMI and AHI was analysed as well. After sleep registration sleep endoscopy was performed to detect the level(s) of obstruction. This gives information about local causes of obstruction and is obtained with induction of sleep by means of midazolam. These results will be presented in the second part of this paper (Chapter 3) .

Sleep endoscopy was not performed in severe OSAS patients. The reasons are twofold. In the first place we feel that in these cases the use of Midazolam is not justified, since it could be dangerous, while secondly the results of surgery in patients with higher indices are worse and nasal continuous airway pressure (NCPCP) should be offered to these patients, as discussed in the second part of this article. These severe OSAS patients were referred to the pulmonologist for (NCPAP). Patients with alcohol abuse and allergic rhinopathy were excluded.

Results

From the 380 patients who underwent sleep registration 208 patients (54.7 %) had OSAS (95% C. I. 50-60). In 337 of 380 patients, the medical charts confirmed the presence or absence of apnoea complaints (table 1). In 280 of the 380 patients, medical charts confirmed information about hypersomnia complaints (table 2).

From 263 patients medical charts contained both apnoeas and hypersomnia complaints (table 3a and 3b).

The BMI varied from 18.5 – 48.1 kg / m^2 (median 27.5 kg / m^2). We also analysed the relation between the BMI and the AHI (graph 1). The correlation coefficient is 0.31 with a p value of < 0.0001.

The next graph shows age in years against AHI (graph 2). The correlation coefficient is 0.18 with a p value of < 0.0001.

Discussion and Conclusion

This study demonstrates that 54.7 % of our patients with SUS had an AHI > 15 at sleep registration. This is a little bit higher than the frequency reported earlier in the literature (46.7%). Our values specifying OSAS or severe OSAS are the upper values selected from different literature sources.

To distinguish between SUS with- and without OSAS and to select patients in whom further diagnostic work-up and subsequent treatment is needed, a questionnaire as well as various forms of sleep registration have been propagated. Unfortunately, the alternative method for detecting OSAS by noting the apnoea and/or hypersomnia symptoms in SUS-patients, has repeatedly been shown to be inaccurate [23,28,29,32,33]. An alternative diagnostic screening method for OSAS presently evaluated is the acoustic screening test [34,35]. Its value and reliability has to be evaluated in larger series.

In our study 8 patients with OSAS would have been missed when only a history was taken (table 3b). The BMI of these patients varied from 22 to 38 kg/m^2. Three patients had a normal BMI, and two patients had an upper normal BMI and three patients had a BMI > 25. Therefore, introducing the BMI as a third selection criteria is not reliable.

Graph 1 shows that all patients with severe OSAS, with one exception, had a BMI over 25 kg/m^2. The conclusion in our population is that adiposity predisposes to severe OSAS and vice versa; patients with normal weight rarely have severe OSAS. This is the only selection criteria in our study that can predict to some extent the outcome of the sleep registration.

Finally, based on graph 2 it can be concluded that the risk of a high AHI increases with age. This outcome confirms the presumption made in an earlier study done in which only questionnaires were used [36].

Our study shows that even by combining symptoms suggestive of OSAS from the history, no reliable differentiation between SUS with- and without OSAS can be obtained.

In conclusion, sleep registration remains the gold standard. Reasons for not performing it are the costs, the inconvenience, insufficient capacity, long waiting time and labour intensity. The present study suggests however that there are no qualitatively equivalent alternatives to it. In our institution nowadays sleep registration is gradually developing into the cornerstone of the diagnostic work up in SUS.

Acknowledgements

The authors thanks Mr. Guus Hart for his statistical advise and Dr. G. A. G. Davies for his linguistic assistance.

Table 1 Predictive value of history apnoea with the sleep registration outcome

	Apnoea +	Apnoea -	Total
OSAS +	178	15	193
OSAS -	125	19	144
Total	303	34	337

Sensitivity:	178 / 193 = 0.92
Specificity:	19 / 144 = 0.13
Predicting value of a positive test:	178 / 303 = 0.59
Predicting value of a negative test:	19 / 34 = 0.56

Table 2 Predictive value of history hypersomnia with the sleep registration outcome

	Hypersomnia+	Hypersomnia-	Total
OSAS +	45	110	155
OSAS -	35	90	125
Total	80	200	280

Sensitivity:	45 / 155 = 0.29
Specificity:	90 / 125 = 0.72
Predicting value of a positive test:	45 / 80 = 0.56
Predicting value of a negative test:	90 / 200 = 0.45

Table 3a Predictive value of history apnoea and hypersomnia with the sleep registration outcome

	Apn+/ Hyps+	Apn- / Hyps–	Apn- / Hyps+	Apn- / Hyps-	Total
OSAS+	39	98	4	8	149
OSAS –	26	70	3	15	114
Total	65	168	7	23	263

Line 1

Sensitivity: 39 / 149 = 0.26
Specificity: 88 / 114 = 0.77
Predicting value of a positive test: 39 / 65 = 0.60
Predicting value of a negative test: 88 / 198 = 0.44

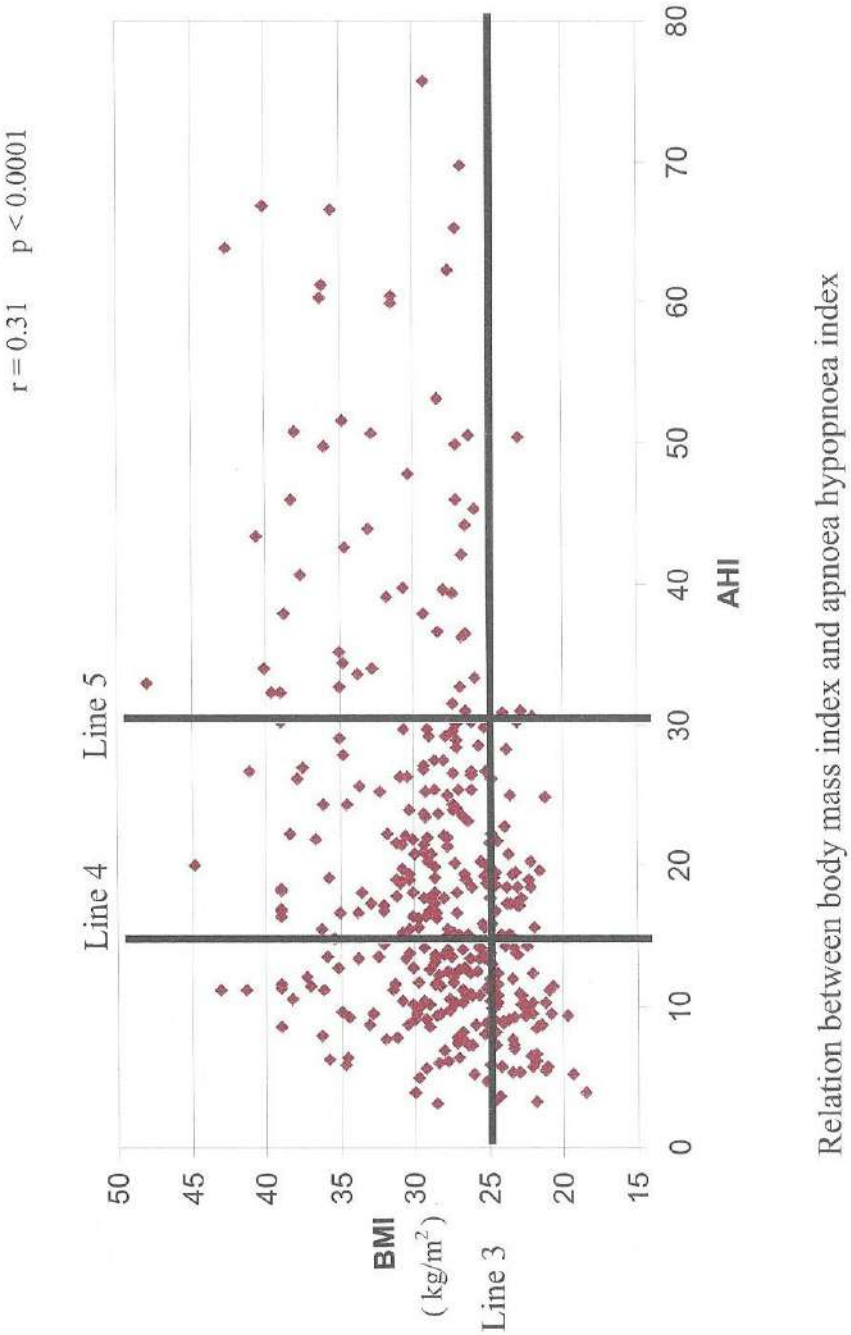
Table 3b Predictive value of history apnoea and hypersomnia with the sleep registration outcome

	Apn+/ Hyps+	Apn- / Hyps–	Apn- / Hyps+	Apn- / Hyps-	Total
OSAS+	39	98	4	8	149
OSAS –	26	70	3	15	114
Total	65	168	7	23	263

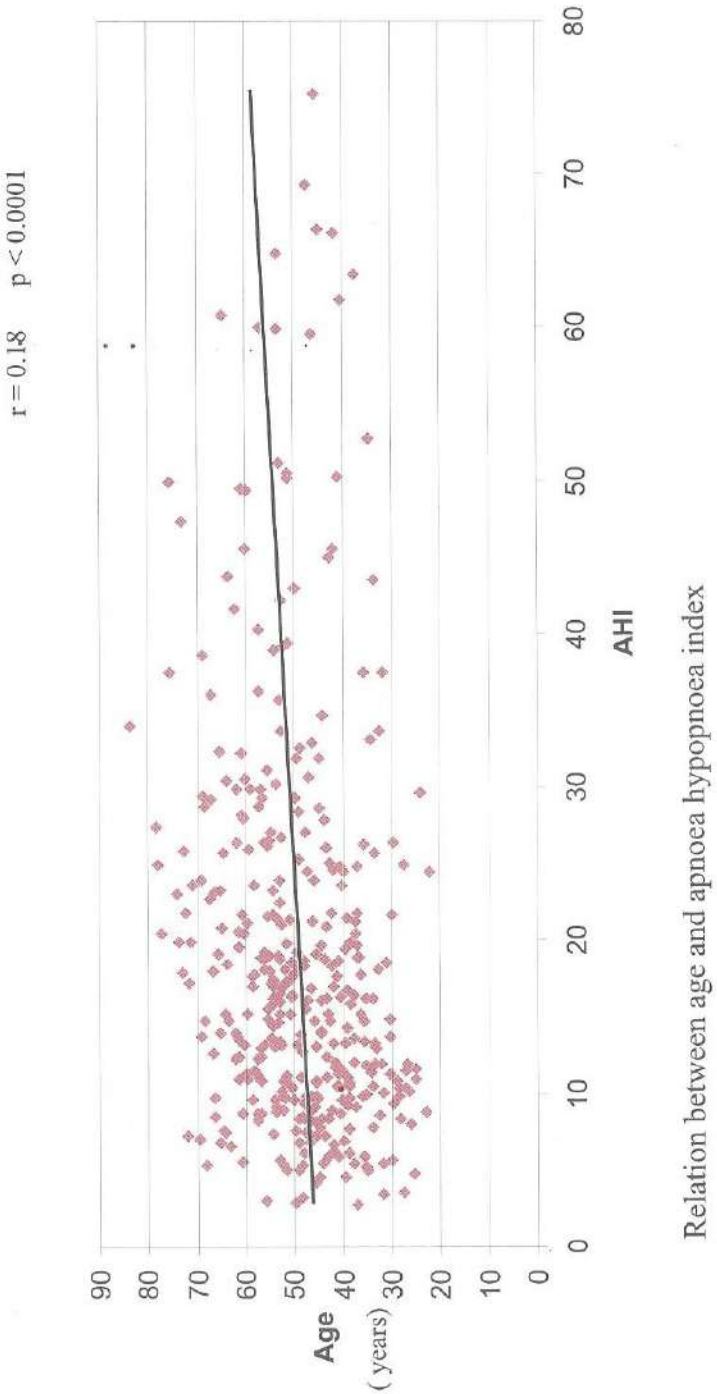
Line 2

Sensitivity: 141/ 149 = 0.95
Specificity: 15 / 114 = 0.13
Predicting value of a positive test: 141/ 240 = 0.59
Predicting value of a negative test: 15 / 23 = 0.65

Graph 1



Relation between body mass index and apnoea hypopnoea index



Graph 2

Relation between age and apnoea hypopnoea index

Literature

1. Gislason T, Almqvist M, Eriksson G, Taube A, Boman G. (1988). Prevalence of sleep apnoea syndrome among Swedish men - an epidemiological study. J Clin Epidemiol 41: 571-576.
2. Norton PG, Dunn EV. (1985). Snoring as a risk factor for disease: an epide-miological survey. Br Med J (Clin Res Ed) 291(6496): 630-62.
3. Fitzpatrick MF, Martin K, Fossey E, Shapiro CM, Elton RA, Douglas NJ (1993). Snoring, asthma and sleep disturbance in Britain: a community based survey. Eur Respir J 6: 531-535.
4. Stradling JR, Crosby JH. (1991). Predictors and prevalence of obstructive apnoea and snoring in 1001 middle aged men. Thorax 46: 85-90.
5. Lugaresi E, Cirignotta F, Coccagna G, Piana C. (1980). Some epidemiologi-cal data on snoring and cardiocirculatory disturbances. Sleep 3(3-4):221-224.
6. Koskenvuo M, Kaprio J, Partinen M (1985). Snoring as a risk factor for hypertension and angina pectoris. Lancet 331: 893-896.
7. Knuistingh Neven A, Middelkoop HAM, Kemp B, Kamphuisen HAC, Springer MP. (1998). The prevalence of clinical significant sleep apnoea syndrome in the Netherlands. Thorax 53(8): 638-42.
8. Woodhead CJ, Davies JE, Allen MB (1991). Obstructive sleep apnoea in adults presenting with snoring. Clin Otolaryngol 16: 401-5.
9. Cirignotta F, D'Alessandro R, Partinen M, Zucconi M, Cristina E, Gerardi R, Cacciatore FM, Lugaresi E. (1989). Prevalence of every night snoring and obstructive sleep apnoeas among 30-69-year-old men in Bologna, Italy. Acta Neurol Scand 79(5): 366-72.
10. Browman CP, Sampson MG, Yolles SF, Gujavarty KS, Weiler SJ, Walsleben JA, Hahn PM, Mitler MM. (1984). Obstructive sleep apnoea and body weight. Chest 85(3): 435-8.
11. Nieto FJ, Young TB, Lind BK, Shahar B, Sarnet JM, D´Agostino RB, Newman AB, Lebowitz MD, Pickering TG. (2000). Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 283(14): 1829-36.
12. Taasan VC, Block AJ, Boysen PG, Wynne JW. (1981). Alcohol increases sleep apnoea and oxygen desaturation in asymptomatic men. Am J Med 71(2): 240-5.
13. Dolly FR, Block AJ.(1982). Effect of flurazepam on sleep-disordered breathing and nocturnal oxygen desaturation in asymptomatic subjects. Am J Med 73(2): 239-43.

14. Bonora M, St. John WM, Bledsoe TA. (1985). Differential elevation by protriptyline and depression by diazepam of upper airway respiratory motor activity. Am Rev Respir Dis 131(1): 41-5.
15. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. (2000). Longitudinal study of moderate weight change and sleep disordered breathing. JAMA 284(23): 3015-21.
16. Sher AE, Trophy MJ, Shprintzen RJ, Spielman AJ, Burack B, Mc Gregor PA. (1985). Predictive value of Mueller Manoeuvre in selection of patients for uvulopalatopharyngoplasty. Laryngoscope 95: 1483-1487.
17. Boot H, Poublon RML, Van Wegen R, Boogaard JM, Schmitz PI, Ginai AZ, Van der Meche FG. (1997). Uvulopalatopharyngoplasty for the obstructive sleep apnoea syndrome: value of polysomnography, Mueller manoeuvre and cephalometry in predicting surgical outcome. Clin Otolaryngol 22(6): 504-10
18. Pringle MB, Croft CB. (1991). A comparison of sleep endoscopy and the Mueller manoeuvre. Clin Otolaryngol 16: 559-562.
19. Croft CB, Pringle M. (1991). Sleep endoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol 16: 504-9.
20. Pringle MB, Croft CB. (1993). A grading system for patients with obstructive sleep apnoea – based on sleep endoscopy. Clin Otolaryngol 18: 480-4.
21. Marais J. (1998). The value of sedation endoscopy: a comparison between snoring and non-snoring patients. Clin Otolaryngol 23: 74-6.
22. Johns MW. (1991). A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 14: 540-45.
23. Osman EZ, Osborne J, Hill PD, Lee BWV. (1999). The Epworth Sleepiness Scale: can it be used for sleep apnoea screening among snorers? Clin Otolaryngol 24: 239-41.
24. Lim PVH, Curry AR. (2000). The role of history, Epworth Sleepiness Scale Score and body mass index in identifying non-apnoeic snorers. Clin Otolaryngol 25: 244-48
25. Ferber R, Millman R, Coppola M, Fleetham J, Murray CF, Iber C, McCall V, Nino-Murcia G, Pressman M, Sanders M. (1994). Portable recording in the assessment of sleep apnoe: ASDA standards and practice. Sleep 17: 372-7.
26. Douglas NJ, Thomas S, Jan MA. (1992). Clinical value of polysomnography. Lancet 339: 347-350.
27. Rollheim J, Osnes T, Miljeteig H. (1999). The site of obstruction in OSA. identified by continues measurement of airway pressure and flow during sleep: ambulatory versus in-hospital recordings. Clin Otolaryngol 24: 502- 506.

28. Chervin RD, Aldrich MS. (1999). The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnoea. Neurology 52: 125-131
29. Kingshott RN, Sime PJ, Engleman HM, Douglas NJ. (1995). Self assessment of daytime sleepiness: patient versus partner. Thorax 50: 994-5.
30. ASDA (1997). Standards of practice: The indications for polysomnography and related procedures. Sleep 20(6): 423-487.
31. Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB Kasper DL, Hauser SL, Longo DL. (1998). Harrison´s principles of internal medicine. 14th edition. Fauci AS. New York- USA.
32. Goh YJ, Choy DKS. (2000). Omission of polysomnography in treatment of snoring: common reasons and medicolegal implications. J Laryngol Otol 114: 519-521.
33. Simmons FB, Guilleminault C, Miles LE. (1984). The palatopharyngoplasty operation for snoring and sleep apnoea: an interim report. Otolaryngol Head Neck Surg 92: 375- 380.
34. McCombe AW, Kwok V, Hawke WM.(1995). An acoustic screening test for obstructive sleep apnoea. Clin Otolaryngol 20: 348-351.
35. Perez-Padilla JR, Slawinski E, DiFransesco LM, Feige RR, Remmers JE, Whitelaw WA. (1993). Characteristics of the snoring noise in patients with and without occlusive sleep apnoea. Am Rev Respir Dis 147: 635-644.
36. Schmitt FA, Phillips BA, Cook YR, Berry DTR, Wekstein DR. (1996). Self report of sleep symptoms in older adults: correlates of daytime sleep iness and health. Sleep 19(1): 59-64.

Chapter 3

Diagnostic work up of socially unacceptable snoring.

Sleep endoscopy

Natascha S Hessel MD (1),
Nico de Vries, MD PhD (1)

(1) Department of Otorhinolaryngology/
Head and Neck Surgery, Saint Lucas Andreas
Hospital, Amsterdam, The Netherlands
NS Hessel, resident,
N de Vries, otorhinolaryngologist

Eur Arch Otorhinolaryngol 2002 Mar;259(3):154-7

Abstract

In the diagnostic work-up of socially unacceptable snoring with or without a history suspicious of OSAS, one should be informed of the severity of the pathology as well as of local and general causative factors. In part I of this study, we reported on the findings in 380 patients by means of sleep registration. In this part, we emphasise on analysis of the local contributing factors. In 340 of the 380 patients sleep endoscopy was performed in order to establish as accurately as possible the level(s) of obstruction. Sleep endoscopy was performed by artificial induction of sleep by Midazolam and consisted of endoscopy and flexible nasopharyngoscopy and laryngoscopy. Although obstruction at oropharyngeal level was often present, lower levels or combinations of levels of obstruction were frequently found as well. In many cases sleep endoscopy showed different level(s) of obstruction than suspected by means of ear nose and throat (ENT) investigation only. An obstruction at only one level was registered in 35 % of the patients (119), while 65 % of patients (221) had multilevel obstruction. The level(s) of obstruction could be well established by sleep endoscopy. We conclude that a diagnostic work-up by means of a combination of sleep registration, sleep endoscopy, and analysis of general factors is worthwhile. By combining the results of these tests, an individually tailored treatment advice can be given.

Key words

Obstructive sleep apnoea syndrome • Sleep endoscopy • Sleep registration • Snoring

Introduction

Both local and general factors contribute to snoring and OSAS [1]. Local causes can be divided into four levels of obstruction: I) nose and nasopharynx, II) oropharynx, III) hypopharynx and IV) larynx. Multiple levels of obstruction are often present. Anatomic causes of nasal and nasopharyngeal obstruction include nasal septum deviation, hypertrophic inferior conchae, nasal polyps and adenoid hypertrophy. Obstruction at oropharyngeal level can be caused by tonsillar enlargement, a long uvula, inadequate patency at the level of the soft palate and/or redundant lateral pharyngeal tissue. Obstruction at hypopharyngeal - laryngeal level (epiglottis,base of the tongue and lateral pharyngeal tissue) is less often present.

Routine ear nose and throat (ENT) examination of the awake patient in a sitting position gives limited information because throat muscles relax during sleep, distorting the anatomy of the awake. The same is true for the Mueller manoeuvre [2-4]. More reliable information about local causes of obstruction can be obtained with sleep endoscopy during artificial induction of sleep by means of midazolam or propofol [4-9].

The purpose of this study is to evaluate the local causative factors in 340 socially unacceptable snorers (SUS) by means of sleep endoscopy and to compare them with previous studies. In part I we discussed the significance of the sleep registration to determine the presence and severity of the obstructive sleep apnoea syndrome (OSAS). The ultimate goal of our method of work-up is to develop an individually tailored treatment programme, based on the combined information obtained by sleep registration, sleep endoscopy and analysis of general factors.

Materials and methods

Patients who were seen between February 1995 and April 1999 with (at least) SUS were retrospectively studied. At the first visit and after routine ENT-examination, they were scheduled for sleep registration, while the majority of these patients had in addition sleep endoscopy with midazolam. Patients with severe sleep apnoea (apneu index > 20, apneu-hypopneu index >30), severe obesity, patients who already had had surgery of the upper airways for snoring or OSAS, patients with a short history of snoring, patients with obvious alcohol abuse, or seasonal nasal obstruction by allergic rhinopathy, were excluded from sleep endoscopy. For dynamic sleep research with midazolam, patients only qualify with ASA (American Society of Anaesthesiologists) classification I (the patient is healthy) and II (an illness or abnormality with a minor effect on the common state, for example: hypertension).

In dynamic sleep nasendoscopy anatomy of the nose, nasopharynx, oropharynx, hypopharynx and larynx were studied by means of a flexible endoscope. The level of obstruction and soft tissue collapse were noted.

Preceding the dynamic sleep endoscopy the nose and nasopharynx were sprayed with a local anaesthetic and decongestive (xylomethazoline and tetracaine 1%). The investigation took place in supine position and if necessary on the left or right side. We used midazolam starting with 0.07 mg/kg bodyweight to a maximum of 0.1 mg/kg.

Results

The snoring group consisted of 297 males and 83 females in an age range from 22 - 82 years (median and mean 49). Bodyweight: the Body Mass Index (BMI) ranged from 18.5 till 48.1 kg/m^2 (median 27.5; mean 28.5; SD 5). A BMI from 25 kg/m^2 is defined as obesity. While all 380 patients received nocturnal sleeping registration, 340 patients underwent endoscopy and flexible nasopharyngoscopy and laryngoscopy with midazolam sedation.

Sleep endoscopy (level of obstruction)

340 patients received sleep endoscopy; 119 patients (35%) had obstruction on one level, 221 patients (65%) on several levels, with in many cases total obstruction at one level and at a second level a minor or partial obstruction. Obstruction at oropharyngeal level was most often present (table 1).

In particular patients with obstructions at hypopharyngeal level and with multi segmental obstruction suffered frequently from OSAS. During endoscopy with sedation none of the patients developed O2-desaturation requiring treatment with Anexate.

Our findings were compared with the Quinn [7] and the Pringle & Croft study [5] (table 1).

Discussion

We analysed how many patients with SUS also had OSAS and which local and general factors play a causative role in it. A number of methods have been evaluated to provide information about local factors of obstruction, including the Mueller manoeuvre, lateral cephalometry [10-13], CT/MRI scanning [14-17], somnofluoroscopy [18], pharyngeal pressure measurements during sleep [19,20] and sleep endoscopy. All diagnostic tests have specific advantages and disadvantages[21].

In the study from Croft and Pringle [4] the Mueller manoeuvre achieved only a 55 % success rate in identifying the velopharyngeal level as the main site of obstruction.
Cephalometry is widely available, easily performed, not as expensive as CT/MRI, but provides limited information about anterior-posterior structures and no information about lateral soft-tissue structures and can not be performed while the patient is sleeping.
CT-scanning is widely available, gives accurate assessment of upper-airway cross sectional area and volume, is potentially useful in the evaluation of sleep apnoea patients who undergo bony manipulation, but is relatively expensive and radiation exposure limits ability to perform repeat studies awake and a sleep.
MRI gives an accurate assessment of the upper airway cross-sectional area and volume, is without radiation and has an excellent airway and soft-tissue and fat resolution, but is expensive and is hard to perform during sleep.
Somnofluoroscopy which has the disadvantage of considerable radiation, has still to be established in greater series as a diagnostic tool.
"Rhinosleep" -which is based on acoustic reflectometry which consist of measurement of pressure difference (level of obstruction) on oropharyngeal and hypopharyngeal levels by means of a nasogastrical pressure tube - might be promising but is still under investigation.
Also pharyngeal pressure measurement during sleep to detect the level(s) of obstruction needs further investigation.
Although it is laborious, sleep endoscopy has been suggested to be the best available method to identify the site of snoring in a general ENT-practice [3-8,22]. Endoscopy during artificially induced sleep approaches the situation during snoring. There are two methods to induce the sleeping situation: intravenous administration of propofol, or intravenous administration of midazolam. In the Netherlands, guidelines were recently developed to give sedation safely by a doctor who is not an anaesthetist [23]. This procedure should only be done on patients with ASA classification I (the patient is healthy) and II (an illness or abnormality with a minor effect on the common state, for example: hypertension). The doctor who performs the procedure has to have knowledge about the pharmacology, supporting medical personnel, monitoring, data management, recovery and aftercare. In our experience, the method is feasible and is now routinely performed. Usually, it shows the level(s) of obstruction clearly and in many, but not all cases, snoring itself can be visualised in a dynamic setting. Although serious complications of intravenous application of midazolam have been reported, (24) we have not encountered such serious problems. In none of the patients has the use of the antidote (flumazenil) been necessary. We believe that this is due to the fact that we have strict exclusion criteria for intravenous administration of midazolam, including severe obesity, obvious alcohol abuse and ASA classification > II. In patients with an apneu index > 20 or apneu-hypopneu index > 30 we do not perform sleep endoscopy either. The reasons are twofold. In the first place we feel that in these cases the use of midazolam is not justified, since it could be dangerous, while secondly the results of surgery in patients with higher indices are worse. We feel that nasal continuous airway pressure (NCPCP) should be offered to these patients.
In 35 % of our patients we saw an obstruction at one level while the numbers in the Quinn- and Pringle/ Croft study were 80 %, 47 % respectively. The reason might be due to the subjectivity of this test and the size of our study.
In 82% of our patients we saw at least obstruction at oropharyngeal level, but a considerable number of patients showed obstruction at other levels as well. This frequency is comparable with the Quinn and Pringle & Croft studies who found 90% and 87% obstruction at oropharyngeal level, respectively.
Obstruction at the hypopharyngeal level was found in our study, the Quinn and Pringle & Croft study in 35%, 22%, 74%, respectively. We were unable to confirm that obstruction at hypopharyngeal level occurs as frequently as found in the last study. Again the subjectivity of this test and the size of our study can be put forward as explanation for the different numbers.
Although there are other studies on sleep endoscopy (4,7-9), these are not comparable, because they were either performed in a different way or the levels of obstruction were not the principal issue of investigation.
After a careful diagnostic work up, which covers several general factors as well as local factors and determination of the severity, an individual treatment advice can be given (diagram 1). Surgical correction should be limited to determined abnormal anatomy and function. Our surgical results based on this philosophy will be reported elsewhere.
For all levels of obstruction there are measures and/or surgical interventions possible, but the severity of the OSAS determines to a large extent how radical the therapy must be.

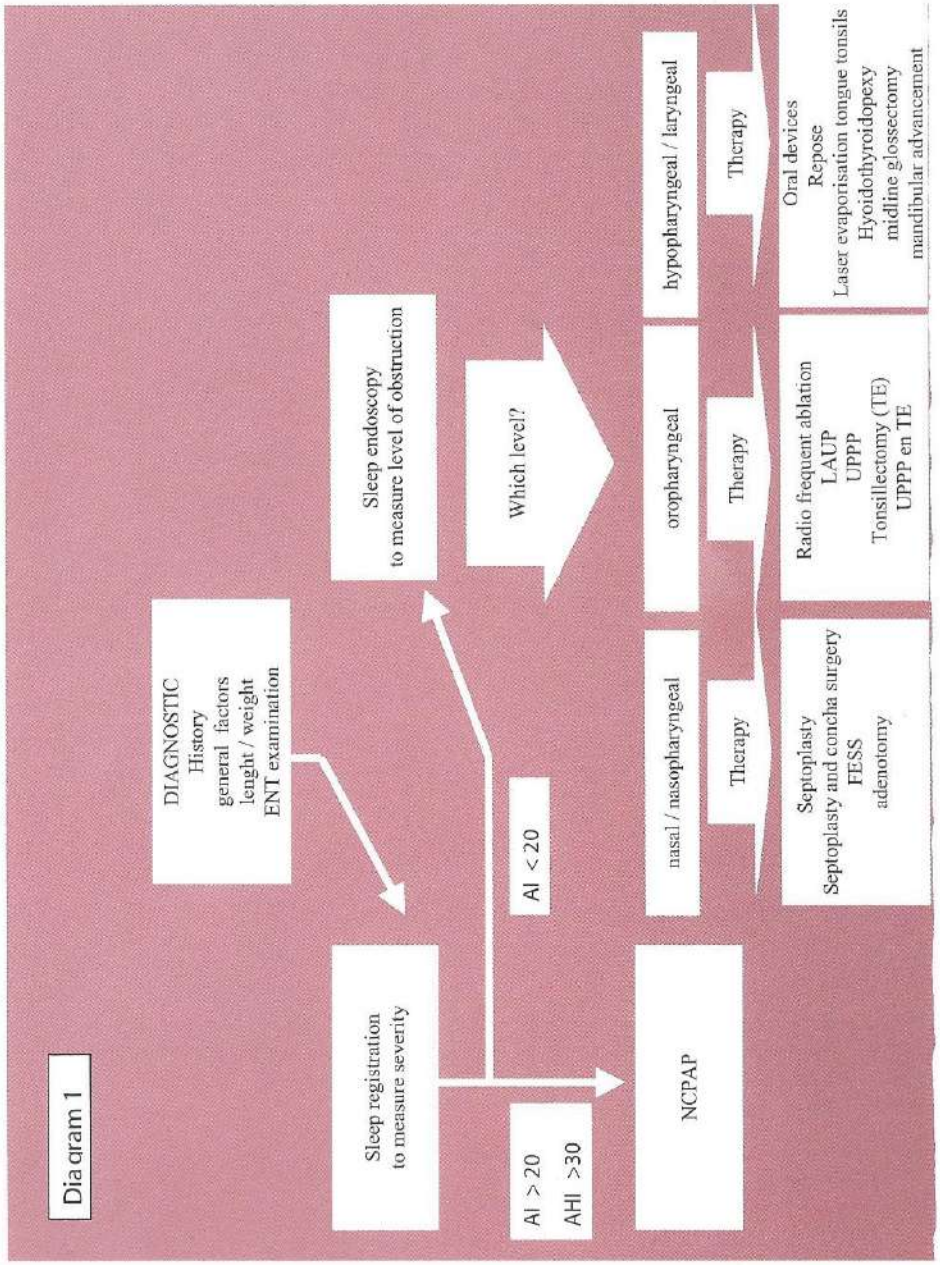
Acknowledgements

The authors thanks Mr. Guus Hart for his statistical advice and Dr. G.A.G. Davies for his linguistic assistance.

Table 1

	Obstruction*	Nasal	Adenoid	Uvula-palatal/ Tonsil	Base of the tongue/epiglottis
Present study					
Total 340 patients	One level 119 patients (35 %)	37 (11 %)	0	74 (22 %)	8 (2 %)
	Multi-level 221 patients (65 %)	165 (49 %)	11 (3 %)	205 (60 %)	113 (33 %)
	Total	202 (60 %)	11 (3 %)	279 (82 %)	121 (35 %)
Quinn study					
Total 50 patients	One level 40 patients (80 %)	0	0	35 (70 %)	4 (8 %) / 1 (2 %)
	Multi-level 10 patients (20 %)	0	0	10 (20 %)	1 (2 %) / 5 (10 %)
	Total	0	0	45 (90 %)	11(22%)
Pringle/Croft study					
Total 70 Patients	One level 33 patients (47 %)	0	0	33 (47 %)	0
	Multi-level 37 patients (53 %)	0	0	28 (40 %)	37 (53 %) / 15 (21 %)
	Total	0	0	61 (87 %)	52 (74 %)

*The classification is based on our categories to make them comparable.



Legend to diagram 1

Firstly the nasal airway has to be patent, and if not, corrected. Patients with an AI > 20 and / or AHI > 30 are referred for NCPAP to the pulmonologist. Patients with 0 < AI < 20 and oropharyngeal collapse, in particularly with a long uvula, receive UPPP (with Tonsillectomy if necessary). Patients with a AI < 10 and oropharyngeal collapse are proposed to radio frequent ablation. For patients with obstruction at hypopharyngeal level several other forms of treatment such as an oral device, midline glossectomy, mandibulair advancement or hyoidothyroidopexy is possible.

Literature

1. Keimpema AJM, Vries N de, Visscher F. (1990). The apnoea syndrome i adults. Neth J Med 134(18): 895-9.
2. Sher AE, Trophy MJ, Sphrintzen RJ, Spielman AJ, Burack B, McGregor PA. (1985). Predictive value of Mueller Manoeuvre in selection of patients for uvulopalatopharyngoplasty. Laryngoscope 95: 1483-1487.
3. Pringle MB, Croft CB. (1991). A comparison of sleep endoscopy and th Mueller manoeuvre. Clin Otolaryngol 16: 559-562.
4. Croft CB, Pringle M. (1991). Sleep endoscopy: a technique of assessmen in snoring and obstructive sleep apnoea. Clin Otolaryngol 16: 504-509.
5. Pringle MB, Croft CB. (1993). A grading system for patients with obstructive sleep apnoea – based on sleep endoscopy. Clin Otolaryngol 18: 480-484.
6. Quinn SJ, Daly N, Ellis PD. (1995). Observation of the mechanism of snoring using sleep endoscopy. Clin Otolaryngol & Allied Sciences 20(4): 360-4.
7. Sadaoka T, Kakitsuba N, Fujiwara Y, Kanai R, Takahashi H. (1996). The value of sleep endoscopy in the evaluation of patients with suspected sleep-related breathing disorders. Clin Otolaryngol 21(6): 485-9.
8. Camilleri AE, Ramamrthy L, Jones PH. (1995). Sleep endoscopy: what benefit to the management of snorers? J Laryngol Otol 109(12): 1163-5.
9. Marais J. (1998). The value of sedation endoscopy: a comparison betwee snoring and non-snoring patients. Clin Otolaryngol 23: 74-6.
10. Deberry-Borowiecki B, Kukwa A, Blanks RH. (1988). Cephalometric analysis for diagnosis and treatment of obstructive sleep apnoea. Laryngoscope 98 (2): 226-34.
11. Mochizuki T, Okamoto M, Sano H, Naganuma H. (1996). Cephalometri analysis in patients with obstructive sleep apnoea syndrome. Acta Otolaryngol 524: 64-72.
12. Partinen M, Guilleminault C, Quera-Salva MA, Jamieson A. (1988). Ob-structive sleep apnoea and cephalometric roentgenograms. The role o anatomic upper airway abnormalities in the definition of abnormal breathing during sleep. Chest 93(6): 1199-205.
13. Riley R, Guilleminault C, Herran J, Powell N (1983). Cephalometric analysis and flow loops in obstructive sleep apnoea patients. Sleep 6(4): 303-311.
14. Stein MG, Gamsu G, de Geer G, Golden JA,Crumley RL, Webb WR. (1987). Cine CT in obstructive sleep apnoea. AJR 148 (6): 1069-74.
15. Ryan CF, Lowe AA, Li D, Fleetham JA (1991). Three-dimensional upper airway computed tomography in obstructive sleep apnoea. Am Rev Respir Dis 144: 428-32.
16. Suto Y, Matsuo T, Kato T, Hori I, Inoue Y, Ogawaw S, Suzuki T, Yamada M, Otha Y (1993). Evaluation of the pharyngeal airway in patients with sleep apnoea: Value of ultrafast MR imaging. AJR 160(2): 311-314.
17. Hasegawa K, Nishimura T, Mikio Y, Natsuki M, Nobuhiro S, Kiouchi I. (1996). Diagnosis by dynamic MRI in sleep disordered breathing. Acta Oto-laryngol 523: 29-31.
18. Katsantonis GP, Walsh JK. (1986). Somnofluoroscopy : its role in the selection of candidates for uvulopalatopharyngoplasty. Otolaryngol-Head Neck Surg 94(1): 56-60.
19. Rollheim,J, Osnes,T, Miljeteig,H. (1999).The sites of obstruction in OSA, identified by continuous measurements of airway pressure and flow during sleep: ambulatory versus in-hospital recordings. Clin.Otolaryngol 24: 502-506.
20. Verse T, Pirsig W. (1997). Pharyngeal pressure measurements in topodiagno sis of obstructive sleep apnea. HNO 45(11): 898-904.
21. Schwab RJ. (1998). Upper airway imaging. Clin Chest Med 19: 33-54.
22. Myatt HM, Beckenham EJ. (2000). The use of diagnostic Sleep endoscopy in the management of children with complex upper airway obstruction. Clin Otolaryngol 25: 200-208.
22. Knape JTA, Everdingen JJE (1999) Guideline for administration of sedatives and analgesics by physicians who are not anesthesiologists. National Organisation for quality assurance in hospitals. Neth J Med 143(21): 1098-102.
23. Nozaki-Taguchi N, Isono S, Nishino T, Numai T, Taguchi N. (1995). Upper airway obstruction during Midazolam sedation: modification by nasal CPAP. Can J Anaesth 42(8): 685-90.

Chapter 4

Feasibility study of Flextube reflectometry for localisation of upper airway obstruction in obstructive sleep apnea

Natascha S Hessel MD (1),
Martin Laman MD (2),
Vincent CPJ van Ammers (2),
Hans van Duijn MD PhD (2),
Nico de Vries, MD PhD (1)

(1) Department of Otorhinolaryngology/Saint Lucas Andreas Hospital, Amsterdam, The Netherlands
Head and Neck Surgery,
Saint Lucas Andreas Hospital, Amsterdam,
The Netherlands

(2) Department of Clinical Neurophysiology,
Saint Lucas Andreas Hospital, Amsterdam,
The Netherlands

Rhinology 2003 Jun;41(2):87-90

SUMMARY

One hundred and twenty-three patients with snoring problems and/or obstructive Sleep Apnea Syndrome (OSAS) were offered Rhinosleep Flextube-reflectometry during sleep registration to assess the upper airway. The main point of interest was patient acceptance of the procedure. 36 patients with OSAS received Rhinosleep Flextube-reflectometry. Of these, 19 (53%) completed a whole night registration with the Rhinosleep tube and 17 (47%) did not. This low success rate is multifactorial and will be discussed in detail in the text. The development of Rhinosleep is a challenge, as it improves the topical diagnostic work-up of OSAS patients. At present however various practical problems have to be solved to make it a viable alternative to sleep endoscopy.

Key words:

Obstructive sleep apnea • Diagnosis • Acoustic reflection • Obstruction

INTRODUCTION

The diagnostic work-up of obstructive sleep apnea syndrome (OSAS) and socially unacceptable snoring (SUS) are currently of great interest. To differentiate between these two forms of snoring sleep registration is mandatory and sleep registration is regarded as the golden standard (Faber *et al.*, 1994; Douglas *et al.*, 1992; Hessel *et al.*, 2002a). Many forms of topical diagnostic have been described, such as the Mueller manoeuvre, lateral cephalometry, CT/MRI scanning, somnofluoroscopy, pharyngeal pressure measurements during sleep and sleep endoscopy (Schwab, 1998). We believe that sleep endoscopy is the best form of routine diagnosis presently available to the general ENT specialist and we reported recently on our experiences with it (Camilleri *et al.*, 1995; Quinn *et al.*, 1995; Croft and Pringle, 1995; Hessel *et al.*, 2002b). The advantages are obvious: it is a dynamic diagnostic procedure during sleep, with direct visual information, with almost always accurate information about the level(s) of obstruction, and it often shows snoring and apneas. All three levels of obstruction (nose-nasopharynx, retropalatal level and retrolingual level) can be analysed.

However, the procedure has disadvantages. The endoscopy is only performed for a short period of time, often only one sleeping position is studied, during only one sleep phase, and sedation is not always successful; it costs the patient almost a complete day in order to get awake to regain normal daytime functions. Intravenous sedation with midazolam is not without risk, in particular in patients in poor health and is in case of a high apnea-hypopnea index (AHI) contra-indicated. Some doubt whether artificial induction of sleep reflects natural sleep.

A recent new development is the Rhinosleep, Flextube reflectometry for assessment of the upper airway in OSAS patients (Faber *et al.*, 2001a; Faber *et al.*, 2001b; Miyazaki *et al.*, 2001). If feasible this form of diagnostic work-up could possibly replace sleep endoscopy and other diagnostic tools with many obvious advantages. In this feasibility study, we present our first experiences with it.

MATERIALS AND METHODS

Between January 2001 and January 2002, 170 patients were seen with SUS and OSAS. All patients were scheduled for sleep registration and sleep endoscopy. Preceding the sleep registration it was unknown if the patient was an OSAS patient. The majority of these patients were regarded as suitable for Rhinosleep; excusion criteria were previous retropalatal and retrolingual surgery. The OSAS patients were retrospectively selected for Rhinosleep analyses. An AHI of more than 15 apnoeas per hour established OSAS (Hessel *et al.*, 2002a). The patients were informed about the study objectives and gave written informed consent to participate. The study was approved by the local Medical Ethical Committee. We stressed that the insertion of the tube could be a little uncomfortable, that having the tube *in situ* could be uncomfortable as well, but the procedure could be terminated at will. We explained that one of the parameters under study was acceptance and our advice would be given on the results of sleep registration and sleep endoscopy. We also stressed that it was an additional experimental investigation. Since the tube is meant to detect the level of obstruction during sleep in OSAS patients, we focused only on this group.

THE ACOUSTIC REFLECTION SYSTEM

Rhinosleep Flextube reflectometry

Rhinosleep Flextube reflectometry is a device developed to detect the level(s) of obstruction in patients who have OSAS. It is not meant to detect level(s) of obstruction in SUS patients.

Mini probe

The acoustic device consisted of a portable computer and a Miniprobe; a small and light metal rod (10 cm and 70 g), containing a microphone/telephone and attached to a flexible tube (Rhino Flextube) as shown in Figure 1.

Measuring device

The computer contained a 24-bit digital signal processor (DSP) and an analogue to digital (AID) and digital to analogue (DIA) converter. The digital Signal Processor supply, a continuous white band noise signal characterised by a bandwidth from 125 to 20 000 HZ, to the miniprobe.

Rhino Flextube

The proximal part of the Flextube, placed in the nose, was relatively thick walled (0,7 mm, store 64A, PVC). The distal part of the Flextube (55 cm), which was placed in the pharynx and oesophagus, was thin walled (wall thickness 0,2 mm). It is made of soft PVC (shore 38A). 'Shore' specifies a method for determination of the indentation hardness of plastics and ebonite by means of duro meters of two types: type A is used for softer materials and type D is used for harder materials. The diameter of the Flextube was 4,4 mm. The Flextube was closed at the distal end.

Software/ Sleep registration

The software performed a statistical comparison of the generated noise and the measured noise providing information concerning the internal diameter of the Flextube, the number and the duration when narrowing of the upper airway occurred (Figure 1).

Intubation Rhino Flextube

When the soft palate, the tongue, or other structures of the pharynx narrow the Flextube, its cross-sectional area decreases. This results in a reflection of the sound from the narrowed level. Flextube narrowing, which result in a cross-section area reduction of 16 % or more for at least 10 sec, should be scored as an obstructed event.

The distance from the nostril to the nose was determined by endoscopy in each patient. Preceding the endoscopy the nose and nasopharynx were sprayed with a local anaesthetic and decongestive (xylomethazoline 0,1% and tetracaine 1%). The Flextube was advanced slowly while the patients swallowed some water. The Flextube was fixed to the nose and cheek with the aid of adhesive tape and the 0 point of Flextube was placed exactly at the posterior border of the nasal septum. The tube is for logistic reasons already inserted in the afternoon, while registration only starts at 11.00 P.M. In many patients the tube was already eight hours *in situ*, before registration started. Ideally, the tube should be inserted just before the sleep period and only in OSAS patients.

Sleep registration

Polysomnography was performed on an digital recorder (Embla, Flaga Medical devices, Reykjavik, Iceland) and consisted of electroencephalogram (Fp2/C4, C4/02), electrooculogram (right and left), electrocardiogram, surface electromyography of right anterior tibial muscle, mentalis muscle, and right diaphragm, arterial oxygen saturation and heart rate by pulse oximeter (numerical depicted), thoracoabdominal excursions (piezoelectric transducers), oronasal airflow by thermocouple sensors (Pro- Tech, Woodinville, WA, USA), snoring registration by small microphone attached to the Deck, and a body position sensor (Pro- Tech, Woodinville, WA, USA). Electrodes and sensors were placed and the equipment was calibrated late in the afternoon. The battery-powered system was switched on and off automatically at 7.00 p.m. and 7.00 a.m., respectively. All signals were recorded wilt DDD (digital sampling, digital filtering, digital storage) recording technology, permitting a sample efficiency of 90% and a sample rate up to 200 Hz. Storage was done on a PCMCIA flash-card.

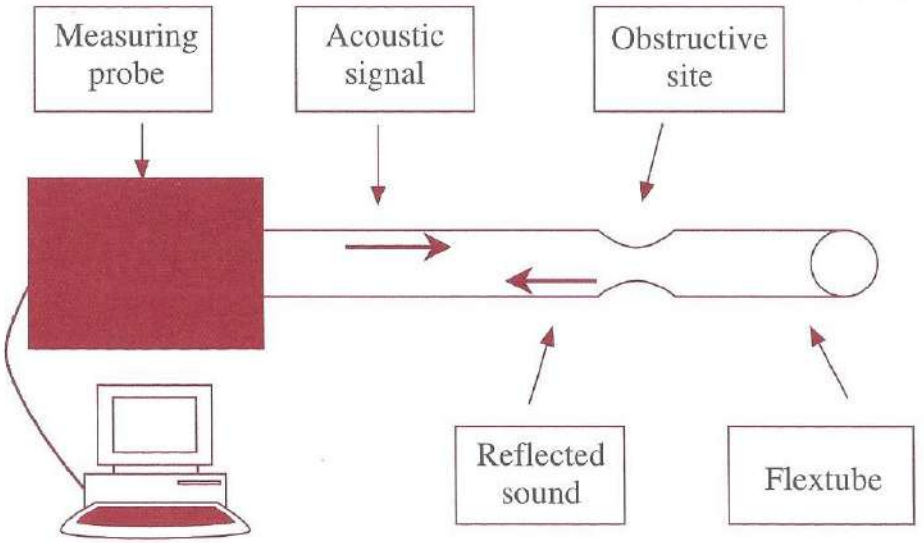


Fig. 1. The flextube reflectometry system. A continuous white band noise was generated in the probe and sent into the flextube. When the flextube was narrowed the noise was reflected. A microphone in the probe recorded the reflected sound. The distance to the flextube narrowing and the duration and degree of the narrowing were calculated by the measuring system and graphically illustrated by the software.

The following day, the data were downloaded, analysed by a dedicated sleep software (Somnologica 2.0.2, Flaga Medical Devices, Reykjavik, Iceland) and manually reviewed by an experienced sleep investigator for final analysis, using 30 second epochs for sleep staging, and 2-minute epoch for apnea detection. A sleep apnea, respectively hypopnea, was detected when a four second(s) interval of the oronasal airflow signal dropped below 22%, respectively 70%, of the reference. The reference was the median value of the amplitude during the last 5 minutes before the event. All apnea/hypopnea events shorter than 10 seconds and longer than 120 seconds were ignored.

Sleep endoscopy

For dynamic sleep research with midazolam, patients only qualify with ASA (American Society of Anaesthesiologists) classification I (the patient is healthy) and II (an illness or abnormality with minor systemic effects, for example: hypertension). In dynamic sleep nasendoscopy anatomy of the nose, nasopharynx, oropharynx, hypopharynx and larynx were studied by means of flexible endoscopy. The level of obstruction and soft tissue collapse were noted. Preceding the dynamic sleep endoscopy the nose and nasopharynx were sprayed with a local anaesthetic and decongestive (xylomethazoline 0,1% and tetracaine 1%). The investigation look place in supine position and if necessary on the left or right side. We used midazolam starting with 0.07 mg/kg bodyweight to a maximum of 0.1 mg/kg.

RESULTS

Between January 2001 and January 2002, 170 patients visited our department for snoring problems. Hundred and twenty-three patients were suitable for standard diagnostic work-up with sleependoscopy and sleepregistration. Rhinosleep reflectometry was offered with the purpose to analyse only OSAS patients by Rhinosleep. Forty-seven patients were not suitable candidates for reasons such as expected lack of motivation and/or cooperation because of language problems, and exclusion criteria as previous retropalatal and retrolingual surgery. Of the remaining 123 patients, there were 63 participants and 60 patients who refused the investigation. In the group of participants, 36 tumed out to be OSAS patients, in whom 19 (53%) had a successful registration. Of the 17 (47%) failures, there were 11 patients who regurgitated the tube during or before registration, 4 patients experienced severe discomfort in the nose leading to removal of the tube, in 2 patients artefacts and/or logistics problem during the night prevented successful analysis. Our findings were compared with the Miyazaki et al. (2001) and the Faber et al. (2001) study (Table 1). We also made a comparison of the advantages and disadvantages of the Rhinosleep Flextube-reflectometry and sleep endoscopy (Table 2 and 3).

	Miyazaki et al	Faber et al	Present study
Patients (N)	16	21	36
Successful participation	13 (81%)	21	19 (53%)
Total failures	3 (19%)	0	17 (47%)
Due to removal	0	0	4 (24%)
Hardware problems/logistics	3 (19%)	0	2 (12%)
Regurgitating	3 (19%) re-inserted	0	11 (64%)

Table 1 Comparison of studies.

Table 2a. Rhinosleep advantages

. In one setting diagnosis of severity of OSAS and localisation of obstruction
. Registration of all sleep phases
. Information about varying obstruction levels possible
. A poor health is no contraindication
. A high AH-index is no contraindication

Table 2b Rhinosleep disadvantages

. No visual information
. In case of multilevel obstruction, only the most dominant obstruction is scored
. Nasal passage is theoretically slightly influenced
. Patient experiences insertion of the tube sometimes troublesome
. Patient experiences the tube *in situ* troublesome
. Patient sometimes regurgitates the tube out
. Logistic problems in terms of time between insertion and registration

Table 3a Sleep endoscopy advantages

. Dynamic investigation
. Direct visual information
. Usually good information about the level of obstruction
. Often obvious about snoring and apneas
. Best available reflection in clinical practice of the situation during sleep
. All three levels of obstruction (nose, retropalata1, retrolingual) are analysed

Table 3b Sleep endoscopy disadvantages

. Only analysis during a short period of time
. (Often) only endoscopy in one position
. Only one sleep phase
. Length of time and inconvenience for patient considerable
. Side effects and risks of sedation with midazolam
. A poor health is a contraindication
. A high AH-index is a contraindication
. Artificial induction of sleep might not be a good reflection of natural sleep
. Sedation is not always successful

DISCUSSION

In this study we present our preliminary experiences with Rhinosleep Flextube reflectometry for assessment of the upper airway in cases of OSAS. The advantages of Rhinosleep are that diagnostic work-up can be performed in only one night of registration, (instead of one night and one day), a complete night can be analysed (instead of only the relative short period of sleep endoscopy), all stages of sleep are being analysed, changes in the level of upper airway obstruction changes during the night and during different sleeping phases will be recorded, while poor health and/or higher AH-indexes are no exclusion criteria for this investigation. SUS patients were felt to be not suitable for Flextube reflectometry, because the system detects an area reduction from the tube of 16% or more for at least 10 seconds. Although SUS patients can have a limited number of apnoeas during sleep registration, simple snoring causes usually an area reduction from the Rhinoflex tube below 16%, lasting less than 10 seconds. The present study was meant as feasibility study. The main problem is that in only 19 of 36 (47%) of the total group of OSAS patients, insertion of the tube was successful and the tube remained *in situ* during the whole night. This low percentage can be explained by various reasons. The low threshold in the way the investigation was explained to the patient, has undoubtedly kept some candidates away. Patients were informed that the Flextube registration was for experimental use only, and that the topical diagnosis of level(s) of obstruction itself was based on the sleep endoscopy findings. The consistency of the tube as used so far might have played a role as well. A tube of softer consistency is presently being developed. The tube was in all cases already 8 Hs *in situ,* before registration started. Finally some patients had nasal discomfort with the tube in situ, because of nasal narrowing. Compared to the 21 patients described by Faber et al (2001b) and the 16 patients by Miyazaki *et al.* (2001), our percentage of successful insertion and complete registration is considerably lower. This is almost certainly due to a combination of differences in patients (in our case SUS and mild OSAS, in the Faber et al (2001b) studies severe OSAS and motivated volunteers). In addition we informed patients that the sleep endoscopy would inform us about obstruction level(s) and that Flextube acceptance was meant as important endpoint of this feasibility study. The threshold to take the tube out was low, patients were not pressed to keep it in when they experienced discomfort by it. We are presently working on solutions on these practical problems in order to increase the success percentage of insertion and remain of the tube during the complete registration.
There might be distinct disadvantages of the Rhinosleep as well. There is no direct visual information, which means that in case of obstruction on retropalatal

level, the site of obstruction remains unclear (uvula, tonsil, palate or circular' while in cases of retrolingual obstruction, exact localisation as to the latera pharyngeal wall, base of the tongue or epiglottis can not be established. Tota obstruction of the airways will not in any case give a reduction of the Rhinc Flextube' tube' s cross-sectional area greater than 25 per cent. The reason for this is the relationship between soft tissues and the stiffness of the Rhino flextube The nasal passage is slightly decreased wilt the tube *in situ,* and this coulc influence the outcome as well. An overview of the advantages and disadvantages of Rhinosleep and sleep endoscopy is given in Table 2 and Table 3.

Presently we are comparing the results of Rhinosleep and of sleep endoscopy or one hand, and with the findings of the Embla recording on the other hand. Only after meticulous comparing the results of Rhinosleep with the golden standards can we assess its exact contribution.

REFERENCES

1. Camilleri AE, Ramamurthy L, Jones PH (1995). Sleep nasendosco-py: what benefit to the management of snorers? J Laryngol Otol 109: 1163-1165.
2. Croft CB, Pringle M (1991). Sleep endoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol 16: 504-509.
3. Douglas NJ, Thomas S, Jan MA (1992). Clinical value of polysomnography. Lancet 339: 347-350.
4. Faber CE, Grymer LF, Norregaard 0, Hilberg 0 (2001). Flextube reflectometry for localisation of upper airway narrowing- a preliminary study in models and awake subjects. Respir Med 95: 631-633.
5. Faber CE, Hilberg 0, Jensen FT, Norregaard 0, Grymer L (2001) Flextube reflectometry for determination of sites of upper airway narrowing in sleeping obstructive sleep apnoea patients. Respir Med 95: 639-648.
6. Ferber R, Millman R, Coppola M, Fleetham J, Murray CF, Iber C, McCall V, Nino-Murcia G, Pressman M, Sanders M (1994). Portable recording in the assessment of sleep apnoe: ASDA stan-dards and practice. Sleep 17: 372-377.
7. Hessel NS, Laman MD, Arnmers VCPJ van, Duijn H van, Vries de N (2002a). Diagnostic work up of socially unacceptable snoring. Part I; History or sleep registration. Eur Arch Otorhinolaryngol 259: 154-157.
8. Hessel NS, Vries de N (2002b). Diagnostic work up of socially unacceptable snoring: Part II; Sleep endoscopy. Eur Arch Otorhinolaryngol 259: 158-161.
9. Miyazaki S, Tanaka T, Itasaka Y, Ishikawa K (2001). A trial study of Rhino sleep for the diagnosis of sleep apnea. Psych Clin Neurosciences 55: 249-250.
10. Quinn SJ, Daly N, Ellis PDM (1995). Observation of the mechanism of snoring using sleep nasendoscopy. Clin Otolaryngol 20: 360-364.
11. Schwab RJ. (1998). Upper airway imaging. Clin Chest Med 19: 33-54.

Results of uvulopalatopharyngoplasty after diagnostic work-up with polysomnography and sleep endoscopy; a report of 136 snoring patients.

Natascha S Hessel MD,
Nico de Vries, MD PhD,
Department of Otorhinolaryngology/ Head and Neck Surgery, Saint Lucas Andreas Hospital, Amsterdam, The Netherlands

NS Hessel, resident,
N de Vries, otorhinolaryngologist

Eur Arch Otorhinolaryngol 2003 Febr;260(2):91-5

Abstract

We subjectively and objectively evaluated 136 patients with socially unacceptable snoring (SUS) or obstructive sleep apnoea syndrome (OSAS) treated with uvulopalatopharyngoplasty (UPPP) after diagnostic work-up by sleep registration (polysomnography, PSG) and sleep endoscopy. Of the 136 patients there were 88 with OSAS, and 48 with SUS. The results of the procedure were considered subjectively to be an improvement in 38 (79%) of the SUS patients and in 74 (84%) of the patients with OSAS.

In 36 (40 %) of the 88 patients with OSAS, repeating PSG postoperatively was considered unnecessary because of obvious improvement. Of the 52 patients with a measurement after UPPP, a decrease in apnoea hypopnoea index (AHI) was found in 38 (73%; median decrease 48%) and AHI dropped below 20 in 32 (62%). Apnoea index (AI) was available in 49 (56%) patients and reduced in 31 (63%; median decrease 73%).

An overall positive result in the 88 patients with OSAS, (combining available data on subjective and objective results) was therefore found in 61 (69%; positive subjective result and AHI <15) or 71 (81%; positive subjective result and decrease in AHI), respectively, depending on definition.

We conclude that after diagnostic work-up by sleepregistration and sleependoscopy, the success rate of UPPP increases as compared to historical controls.

Key words:

Snoring • Obstructive sleep apnoea syndrome • Sleep registration • Sleep endoscopy • Uvulopalatopharyngoplasty.

Introduction

The main symptom of the obstructive sleep apnoea syndrome (OSAS) is snoring, often accompanied by daytime sleepiness. OSAS and snoring are associated with increased cardiovascular morbidity and mortality, depression and cognitive problems.[1-6] Simple snoring is present in up till 24% of men and 14% of women.[7-8] Only a minority of snoring patients seek medical advice. However, in a population seeking medical attention in an ear, nose and throat (ENT) practice, sleep registration shows that approximately 50% of these patients have OSAS.[8-9] It is estimated that OSAS affects 4% of males and 2% of females in a cohort of employed 30- to 60 years old individuals.[10] This prevalence indicates that a considerable part of the community needs medical attention and it underlines the importance of diagnosing and treating this condition. Uvulopalatopharyngoplasty (UPPP) was first described by Fujita *et al.* in 1981 and at that time represented a major surgical advance in the treatment of snoring and OSAS.[11] The success rate of the UPPP as described in the literature depends on various factors, such as the definition of success, kind of patients (simple snorers versus severe OSAS), and length of follow-up. Often used definitions of success are subjective improvement (symptom scores), a postoperative drop in apnoea-index (AI) or apnoea-hypopnoea-index (AHI) of at least 50% and a reduction of AHI below 15 or 20.[12-13] A meta-analysis by Sher *et al.* gives a response rate according to the definition of a postoperative drop in apnoea-index (AI) of at least 50% and a reduction of AHI below 20 in 41 % of patients after UPPP.[14]

It is likely that an important reason for this disappointing success rate is inadequate patient selection and it strongly suggests that good diagnostic topical work up to localise the site(s) of obstruction and to estimate the severity of the obstructive sleep apnoea syndrome is mandatory to achieve better treatment results. Different diagnostic methods are used to localise the site of obstruction, such as the Mueller manoeuvre, lateral cephalometry, CT/MRI scanning, somnofluoroscopy, pharyngeal pressure measurements during sleep and sleep endoscopy. Sleep endoscopy is considered by some as probably the best available method for identifying the specific site(s) of snoring in a general ENT practice.[15-18] After a diagnostic work-up with sleep registration (to rule out or to confirm the diagnosis OSAS) and sleep endoscopy (to determine the site(s) of obstruction), logical therapeutic advise can be given (Fig. 1)[19]. Previously we reported on our experiences with sleep registration and sleep endoscopy [9,18]. In this study our results of UPPP after sleep registration and diagnostic sleep endoscopy are reported and compared to historical controls in which this kind of diagnostic work up was not performed.

Material and methods

Between April 1995 and November 2000, 447 patients with (at least) socially unacceptable snoring (SUS) were referred to our department. All patients underwent a nocturnal polysomnography while preoperative sleependoscopy was performed in 370 patients. Of those patients 212 (47 %) were suggested to have UPPP and 176 (83 %) of these 212 responded to this advice. The other patients received such advice as to lose weight, or to have nasal surgery, radiofrequency ablation, oral devices, hyoidthyroidpexia[20] or NCPAP. In most cases, sleependoscopy showed that the (main) level of obstruction in this group was not at the retropalatal level. Of the 176 patients receiving the UPPP operation, 136 were qualified for an objective and/or subjective evaluation of the procedure. Forty patients were not included because reasons such as alcoholism, psychiatric problems or medical charts that were incomplete.

Sleepregistration

The sleep registration patients stayed 1 night in the hospital, and we used a CNS-Sleep I/T-8 recorder, which records the sleep architecture (derived from electroencephalogram, eye movements and submental electromyogram), respiration (thoracic and abdominal measurement), oxygen saturation, movements of limbs and the intensity of the snoring. An apnoea / hypopnoea index (AHI) of more than 15 apnoeas/hypopnoeas per h established OSAS and an AHI of more than 30 was graded as severe OSAS [21].

Sleep endoscopy

After sleep registration, sleep endoscopy was performed to detect the level(s) of obstruction. The endoscopy provides information about local causes of obstruction and is obtained with induction of sleep by means of midazolam. Sleep endoscopy was not performed in severe OSAS patients. The reasons are twofold. Firstly, we feel that in these cases the use of midazolam is not justified because of the risk of severe complications, such as hypoxemia. Secondly the results of surgery in patients with higher indices are worse and nasal continuous airway pressure (NCPAP) should be offered to these patients.

Patient selection for UPPP was based on having at least obstruction on the retropalatal level as observed by sleep endoscopy. We made a distinction between one-level and multilevel obstructions[18]. The therapeutic sequence of events in multilevel obstruction is to approach first the obstruction at nasal level, then if improvement is insufficient, secondly the retropalatal level (palate/ uvula/ tonsillair obstruction) is approached and finally, if still necessary, the retrolingual (tongue-base / epiglottis) obstruction.

UPPP-operation

The operation was performed by three surgeons, according to the procedur described by Fujita *et al.* Tonsillectomy was performed at the same time in thos patients who had not undergone this procedure previously. Only one majo complication was seen, which was nasopharyngeal stenosis, necessitatin, revision surgery.

BMI

The body mass index (BMI) was calculated in all patients. A BMI of more tha 25 kg/m^2 was regarded as obesity. Age and sex characteristics were noted (se Table 1 and Table 2).

Subjective parameters

After the UPPP operation the patient's (and/or partner's) opinions regarding th subjective changes of the symptoms were noted, usually 3 to 5 months afte surgery (Table 3).

Objective parameters

Sixty-six (49%) patients had a postoperative sleep registration, which could b compared to the preoperative registration. Reasons not to repeat PSG afte surgery were mainly if the preoperative AH index was already lower than 15 and/or when the subjective results were very good in terms of considerabl decrease in snoring and reduction in day time sleepiness. For two patients PS was not repeated because of refusal (AHI: 17 and 20). We calculated severa criteria for response, namely 1) overall reduction in A(H)I, 2) a percentag post-operative drop of AHI and 3) reduction of AHI below 20.

Results

There were 136 patients who received the UPPP operation of whom 99 underwen both tonsillectomy and the UPPP operation and 37 only UPPP. Of these 13 patients, 88 had measurable OSAS and 48 suffered only from SUS. The patien demographics and baseline characteristics are displayed in Table 2 and Table 3 Results were scored based on a combination of subjective opinion and objectiv results, when available.

Subjective results

Of the 48 SUS patients, the subjective results improved in 38 (79%), while te patients (21%) were dissatisfied with the result. In the dissatisfied group, th BMI (28,3 kg/ m2) was higher than in the satisfied group (26,7 kg/ m^2) and during endoscopy, relatively more obstruction was seen on the level of base

of the tongue. Of the 88 OSAS patients, 74 (84%) reported (subjective) improvement, while 14 (16%) patients did not.

Objective results

Only 14 patients with SUS had a postoperative PSG. In seven of these 14 patients (59%), the AHI decreased (median decrease 67%). In the other 34 SUS patients, PSG was not repeated, because either the doctor, the patient or both considered the improvement in symptoms convincing enough.

Of the 88 patients with a measurable OSAS (AHI≥15), 36 (40%) patients were not reassessed by PSG, because the subjective improvement was sufficiently convincing to either the doctor or the patient. Of the 52 (60%) patients with a reassessment after UPPP, a decrease in AHI was found in 38 patients (73%; median decrease 48%) and AHI dropped below 20 in 32 patients (62%). In 14 patients (27%), AHI remained similar or increased (median 30%).

Of the 38 patients with an objectively measured decrease in AHI, 32 (84%) reported a subjective improvement, while eight of the 14 patients (57%) with an increased AHI reported subjective improvement.

In 33 of the 74 OSAS patients reporting subjective improvement, sleep registration was not repeated. In the other 41 patients, PSG was repeated and no OSAS was found in 22, while in 19, OSAS was still present. In 33 (80 %)of these 41 patients, the AHI decreased (median 48%), while the AHI did not change or increased in only eight patients. In the 14 patients with a subjective unsatisfactory result, post-PSG was not recorded in two. Of the 12 patients with a PSG after surgery, no OSAS was recorded in four, while OSAS was still present in eight. The AHI decreased in six patients and increased in the six others.

The apnoea index was not available in 39 out of the 88 OSAS patients. Of the 49 patients with a reassessment, AI was reduced in 31 patients (63%, median decrease 73%) and increased in 18 patients (37%, median 28%). However, of those 18 patients with an increase, 12 (67%) reported a subjective improvement at the same time. In the 31 patients with a reduction in AI, the subjective improvement was 87%.

We further analysed if there were differences in outcome for unilevel (uvula-palate only) obstruction and multilevel obstruction (base of tongue as well). We were unable to find a clear relation between the level of obstruction(s) and the success rate after surgery (table 4).

An overall positive result in the 88 patients with OSAS, (combining available data on subjective and objective results) was therefore found in 61 (69%; positive subjective result and AHI <15) or 71 (81%; positive subjective result and decrease in AHI), respectively, depending on the definition.

Discussion

UPPP is performed both for simple snoring as well as for snoring as manifestatior of OSAS. Results of UPPP for SUS are reported subjectively - satisfaction of the patient and partner - , while in OSAS in addition to such a subjective score, ar objective score can be evaluated. Our diagnostic work-up consists o polysomnography and sleep endoscopy [9,18], and in this study on 136 UPPPs, we investigated whether this extended work-up leads to results that are better thar historical controls in which such elaborate diagnostics were not performed.

In 38 (79%) of 48 simple snorers, the subjective result was good. This percentage is acceptable. In the 21% in which the results were not good, a relatively higher BMI was recorded, while during endoscopy relatively more obstruction was found at the level of the base of tongue.

Reporting good results depends heavily on the definition used. An overal positive result in the patients with OSAS in our population, (combining available data on subjective and objective results) was found in respectively 61 (69%) o 88 patients, (positive subjective result and AHI <15) or 71 (81%) of 88 patients (positive subjective result and decrease in AHI). This result compares favourably with many other studies in which approximately success rates of 40 to 50 % for OSAS patients and of 70% for patients who snored were found [14].

In our 88 patients with OSAS, the AHI increased in only 14 (16%), and OSAS was still present in only 27 (31 %) patients, although in many of these cases, the AHI was lower postoperatively.

For UPPP failures because of obstruction at the level of the base of tongue as well, the use of hyoid-thyroidpexia remains in reserve. Our experience with this procedure in UPPP failures will be reported elsewhere. However, it is already apparent that after sleep endoscopy, some patients must be informed that success is only likely to be achieved after surgery at two levels.

We conclude that after diagnostic work-up by sleep registration and sleep endoscopy the success rate of UPPP increases as compared to historical controls Some data remain confusing. Contrary to our expectations, we were unable to find clear differences between patients with obstruction at one level (retropalatal) and two levels (retropalatal and retrolingual). In our opinion both for simple snorers as well as for patients with OSAS, findings during sleep endoscopy are useful But the search for optimal prognostic parameters for treatment outcome of UPPP is still ongoing. Possibly combining findings of sleep endoscopy with results of pharyngeal flextube reflectrometry will provide additional predictive data. Our findings with pharyngeal flextube reflectrometry measurements as compared with sleependoscopy data will be published elsewhere.

Table 1. Summary of demographic and pre-operative polysomnographic data (n=136)

n	136
M:F	123 (90%): 13 (10%)
Age	47.4 ± 10.3 years (range 23-71 year)
Weight	87.2 ± 13,2 kg (range 62-132 kg)
BMI	27.8 ± 3.5 kg / m2
Apnoea index	8.7 ± 11.2 apnoeas/ h total sleep time
A / H index	21.7 ± 15.7 apnoeas/ hypopnoeas/ h total sleep time

Table 2. Patient characteristics at diagnosis

	Snorer (n=48)	Snorer + OSAS (n=88)
Male:Female	45:3	78:10
	mean; stdev (range)	mean; stdev (range)
Age	44.7; 9.2 (25-65)	48.8; 10.7 (22-71)
Weight	83.7; 11.3 (66-112)	89.0; 13.7 (62-132)
BMI	27.0; 3.6 (20-36)	28.8; 3.4 (21-40)
Apnoea Index	2.7; 2.6 (0-9)	12.0; 12.6 (0-90)
A/H index	8.2; 4.5 (0-14)	29.0; 14.7 (15-91)

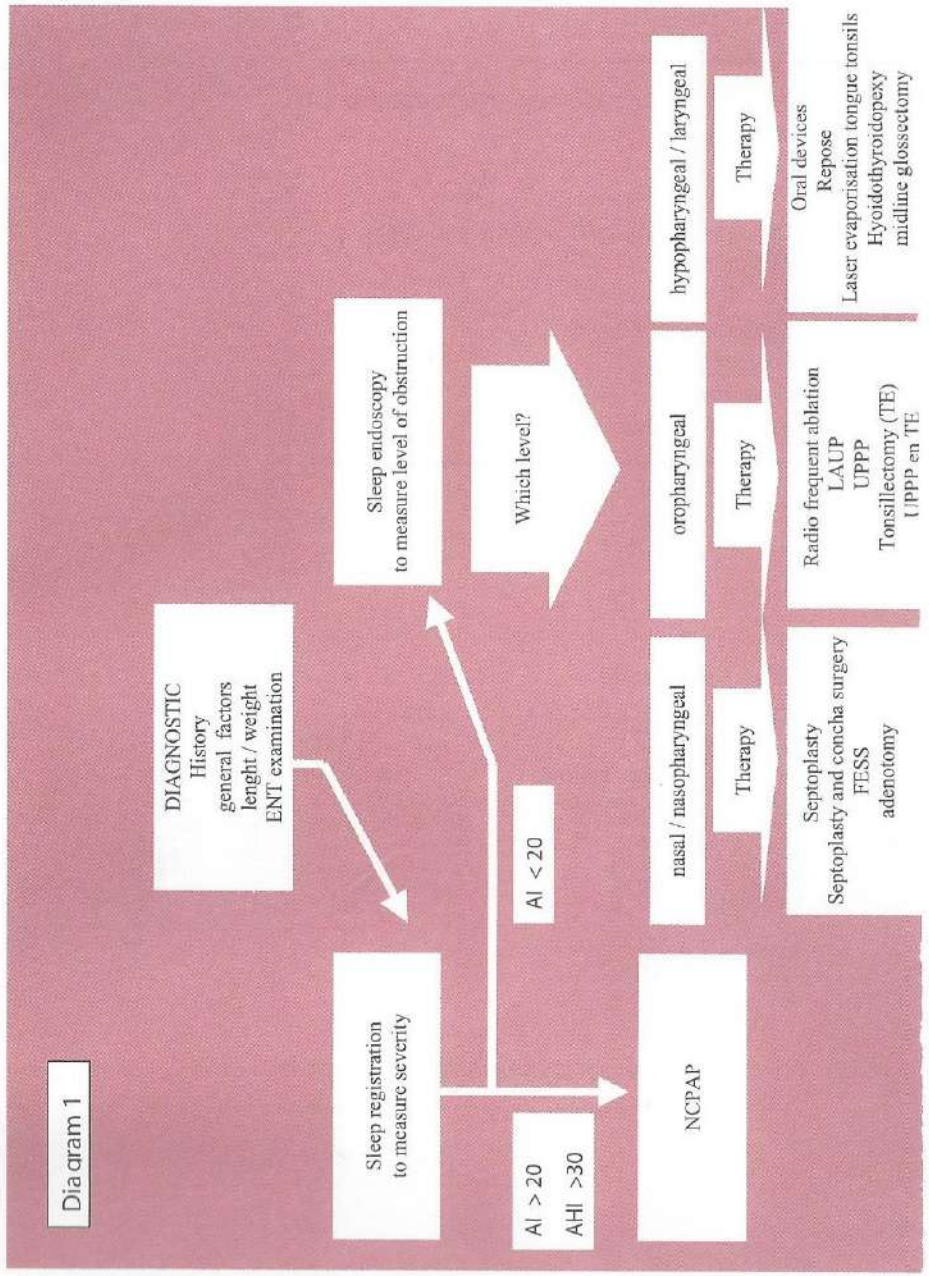
Table 3. Subjective (hetero-) anamnestic opinions after surgery

1. Snoring unchanged
2. No idea
3. More air
4. First snoring decreased, later snoring increased
5. Apnoea still present
6. Less tired
7. Snoring decreased, still tired
8. Snoring decreased
9. Snoring disappeared
10. Patient (family) is satisfied

Table 4 Subjective results type

	Snorer		Snorer + OSAS	
	Wo sening	improvement	wo sening	improvement
level				
I,II	**1**	**9**	**3**	**19**
I,II,III	**3**	**6**	**6**	**16**
II	**4**	**9**	**2**	**13**
II,III	**2**	**12**	**3**	**24**
X	**.**	**2**	**1**	**1**

Legend: I = nasal, II = oropharyngeal, III = hypopharyngeal, X = unknown.



Legend to diagram 1

Firstly the nasal airway has to be patent, and if it is not, it has to be corrected. Patients with an AI > 20 and / or AHI > 30 are referred for NCPAP to the pulmonologist. Patients with 0 < AI < 20 and oropharyngeal collapse, in particularly with a long uvula, receive UPPP (with tonsillectomy if necessary). Patients with an AI < 10, normal uvula, and oropharyngeal collapse are recommended to have radio frequent ablation. For patients with obstruction at hypopharyngeal level, several other forms of treatment such as an oral device, midline glossectomy, mandibulair advancement or hyoidthyroidpexia, are possible.

References

1. Stradling JR, Crosby JH. (1991) Predictors and prevalence of obstructive ap noea and snoring in 1001 middle aged men. Thorax 46: 85-90.
2. Lugaresi E, Cirignotta F, Coccagna G, Piana C. (1980) Some epidemiological data on snoring and cardiocirculatory disturbances. Sleep 3: 221-224.
3. Koskenvuo M, Kaprio J, Partinen M (1985) Snoring as a risk factor for hypertension and angina pectoris. Lancet 331: 893-896.
4. Cirignotta F, D'Alessandro R, Partinen M, Zucconi M, Cristina E, Gerardi R. Cacciatore FM, Lugaresi E. (1989) Prevalence of every night snoring and obstructive sleep apnoeas among 30-69-year-old men in Bologna, Italy. Acta Neurol Scand 79: 366-372.
5. Browman CP, Sampson MG, Yolles SF, Gujavarty KS, Weiler SJ, Walsleben JA, Hahn PM, Mitler MM. (1984) Obstructive sleep apnoea and body weight. Chest 85: 435-438.
6. Nieto FJ, Young TB, Lind BK, Shahar B, Sarnet JM, D'Agostino RB, Newman AB, Lebowitz MD, Pickering TG. (2000) Association of sleepdisordered breathing, sleep apnoea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 283: 1829-1836.
7. Lugaresi E, Cirignotta F, Coccagna G, Piana C. (1980) Some epidemiological data on snoring and cardiocirculatory disturbances. Sleep 3:221-224.
8. Woodhead CJ, Davies JE, Allen MB. (1991) Obstructive sleep apnoea in adults presenting with snoring. Clin Otolaryngol:16:401-405.
9. Hessel NS, Laman MD, Ammers, VCPJ van, Duijn H van, Vries de N. (2002) Diagnostic work up of socially unacceptable snoring. Part I; History or sleep registration. Eur Arch Otorhinolaryngol 259: 154-157.
10. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. (1993) The occurrence of sleep-disorded breathing among middle-aged adults. N Engl J Med 328: 1230-1235.
11. Fujita S, Conway W, Zorick F, Roth T. (1981) Surgical correction of anatomic abnormalities in obstructive sleep apnoea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 89: 923-934.
12. Riley RW, Powell NB, Guilleminault C. (1993) Obstructive sleep apnoea syndrome: 306 consecutively treated surgical patients. Otolaryngol Head Neck Surg 108: 117-125.
13. Hendler BH, Costello BJ, Silverstein K, Yen D, Goldberg A. (2001) A protocol for uvulopalatopharygoplasty, mortised genioplasty, and maxillomandibular advancement in patients with obstructive sleep apnoea: an analysis of 40 cases. J Oral Maxillofac Surg 59: 892-897.
14. Sher AE, Schechtman KB, Piccirillo JF. (1996) An American sleep disorders association review. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnoea syndrome. Sleep 19: 156-177.
15. Camilleri AE, Ramamurthy L, Jones PH. (1995) Sleep nasendoscopy: what benefit to the management of snorers? J Laryngology Otology 109: 1163-1165.
16. Quinn SJ, Daly N, Ellis PDM. (1995) Observation of the mechanism of snoring using sleep nasendoscopy. Clin Otolaryngol 20: 360-364.
17. Croft CB, Pringle M. (1991) Sleep endoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol 16: 504-509.
18. Hessel NS, Vries de N. (2002) Diagnostic work up of socially unacceptable snoring: Part II; Sleep endoscopy. Eur Arch Otorhinolaryngol 259: 158-161.
19. Riley RW, Powell NB, Guilleminault C. (1993) Obstructive sleep apnoea syndrome: a surgical protocol for dynamic upper airway reconstruction. J Oral Maxillofac Surg 51: 742-747.
20. Hsu PP, Brett RH. (2001) Multiple level pharyngeal surgery for obstructive sleep apnoea. Singapore Med J 42: 160-164.
21. ASDA (1997) standards of practice: The indications for polysomnography and related procedures. Sleep 20: 423-487.

Chapter 6

Increase of the apnoea-hypopnoea index after uvulopalatopharyngoplasty: analysis of failure.

Natascha S Hessel MD,
Nico de Vries, MD PhD,

Department of Otorhinolaryngology/ Head and Neck Surgery, Saint Lucas Andreas Hospital, Amsterdam, The Netherlands
NS Hessel, resident,
N de Vries, otorhinolaryngologist

Clin Otolaryngol, accepted

Abstract

From 70 patients who had Uvulopalatopharyngoplasty (UPPP) operation and a pre-and postoperative sleep registration, we could retrospectively determine the failures and the correlation between variables such as age, gender, body mass index (BMI), earlier or concomitant tonsillectomy, unilevel (uvula-palate-tonsil) or multilevel (base of tongue as well) obstruction during sleep endoscopy and treatment outcome.

From 70 patients, the pre-operative sleep registration classified 15 socially unaccepable snorers and 55 obstructive sleep apnoea syndrome (OSAS) patients. In this study we focused on the OSAS patients. From the 55 OSAS patients, 32 were classified as successful after UPPP, because they had a decreased apnoea-hypopnoea index (AHI) after surgery (AHI $\leq$ 20). Eight patients had an decreased AHI, but higher than 20 apnoeas/hyponoeas per hour. Fifteen patients were identified as UPPP failures with an equal or increased AHI and/or subjective deterioration of snoring. We were unable to find a statistically difference between the two groups with respect to variables such as age, BMI and AHI pre-operative (p-value >.56) as between the level of obstruction(s) (p-value >.24). For earlier or concomitant tonsillectomy we found a statistically significant difference (p-value >.039), but a very small number in the high failure group (n = 8).

We conclude that although sleep endoscopy adds to better patient selection and better results, paradoxically, the finding of obstruction on palate-uvula level during sleep endoscopy can still give UPPP failures.

Keywords

Obstructive sleep apnoea syndrome • Uvulopalatopharyngoplasty failure • Sleep endoscopy • Sleep registration.

Introduction

Uvulopalatopharyngoplasty (UPPP) was first described by Fujita *et al* in 1981 and represented at that time a major surgical advance in the treatment of socially unacceptable snoring and obstructive sleep apnoea syndrome (OSAS).[1] The actual success rate for the procedure is a postoperative drop in apnoea-index (AI) of at least 50% and a reduction of apnoea-hypopnoea index (AHI) below twenty (40.7%).[2] We recently showed that this success rate can be improved to at least 62% (with an AHI dropped below 20) by better patient selection by means of a combination of sleep registration and sleep endoscopy.[3-5] After determination of the severity of the AHI and the level(s) of obstruction, an individual tailored advice can be given with improvement of the results after treatment. In the case of socially unacceptable snorers, the level of satisfaction of the patient is a parameter of success. in OSAS patients it is particularly difficult to differentiate only on this subjective experience between success and failure as discussed in Vincini *et al.*[6] The definition of a satisfied OSAS patient is a patient with a reduced snoring and increased feeling of well being. They refer to studies which describe a substantial gap between objective and subjective results (postoperative sleep registration and patient satisfaction, respectively). [7-9] Like other studies [6,10] we also found that after technically successful performance of UPPP, failures can occur, in the sense of an increase in AHI. In the literature it seems there are more speculations than explanations for UPPP failure. Regarding deteriorating results after UPPP, when postoperative sleep registration shows increased AHI and snoring, the literature is scarce. In this study we have retrospectively analysed a group of patients with UPPP failures, to find characteristics that might add to a possible explanation for these negative results.

Patients and methods

We retrospectively reviewed the medical charts (from June 1995 to March 2001) of 140 consecutive patients (Saint Lucas Andreas Hospital) who had UPPP after diagnostic work-up by sleep registration and sleep endoscopy. Seventy of the 140 patients were suitable for objective evaluation of the procedure because they had a pre- and postoperative sleep registration. In the present report, we compare the demographic, (pre-) operative and post-operative data of three groups of patients, responders, failures and failures with an AHI increase of > 35%, to look for possible explanations of these outcomes.

Sleep registration

For sleep registration patients stayed one night in the hospital and we used a CNS-Sleep I/T-8 recorder, which records the sleep architecture (derived from electroencephalogram, eye movements and submental electromyogram), respiration (thoracic and abdominal measurement), oxygen saturation, movements of limbs and the intensity of the snoring. An AHI of more than 15 apnoeas/hypopnoeas per hour established OSAS and an AHI of more than 30 was graded as severe OSAS. [11]

Sleep endoscopy

After sleep registration, sleep endoscopy was performed to detect the level(s) of obstruction. This provides information about local causes of obstruction and is obtained with induction of sleep by means of midazolam. Sleep endoscopy was not performed in severe OSAS patients. The reasons are twofold. Firstly, we feel that in these cases the use of midazolam is not justified because of the risk of severe complications such as hypoxemia. Secondly, the results of surgery in patients with higher indices are worse and nasal continuous airway pressure should be offered to these patients.

Patient selection for UPPP was based on at least obstruction on retropalatal level observed by sleep endoscopy. We made a distinction between one-level and multilevel obstruction.[5] The therapeutic sequence of events in multilevel obstruction is to approach first the obstruction at nasal level, after insufficient improvement, secondly, oropharyngeal level (palate/ uvula/ tonsillair obstruction) and finally if still necessary, the hypopharyngeal (tongue-base / epiglottis) obstruction.

UPPP-operation

The operation was performed by three surgeons, using the procedure described by Fujita *et al.*[1] Tonsillectomy was performed at the same time, in those patients who had not undergone this procedure previously. In only one patient, stenosis at nasopharyngeal level necessitated revision surgery. Other complications have not occurred. Inclusion criteria included medically stable status and significant collapse at least at oropharyngeal level during sleep endoscopy.

Data analysis

Data are presented as mean ± SD, median and the range. The *t*-test was used to compare age, BMI and AHI pre-operative between the two groups (responders and failures after surgery). The chisquared test was used tocompare the level of obstruction and the UPPP with or without the tonsillectomy between the two-groups (responders and failures after surgery). Data were analyzed using Excel, establishing $P < 0.05$ as statistically significant.

Results

Seventy patients had pre-and postoperative sleep registration. All, except five patients had a pre-operative sleep endoscopy. The reasons for not performing the sleep endoscopy were a too high AHI and/or a relatively poor medical condition. From these 70 patients, the preoperative sleep registration classified 15 social snorers and 55 OSAS patients. In this study we focus on the OSAS patients. From the 55 OSAS patients, 32 patients were classified as successful after UPPP (responders), because they had a decreased AHI after surgery (AHI $\leq$ 20). Eight patients had a decreased AHI, but higher than 20 apnoeas/hypopnoeas per hour. As we want to compare the successful defined operated patients with the failures, these eight patients are not described in this study. Fifteen patients were identified as UPPP failures with an equal or increased AHI and/or subjective deterioration of snoring. In this group we made a subgroup of patients with an increased AHI of more than 35 % of the preoperative AHI ($n = 10$). The baseline characteristics and the two groups with respect to the level of obstruction(s) and the operation (with or without tonsillectomy) are shown in Table 1. The difference between the responders and failures (group I and II) concerning age, BMI and AHI preoperative is not statistically significant ($P > 0.56$). We were also unable to find a statistically significant difference ($P > 0.24$) between the two groups with respect to the level of obstruction(s). The difference between the two groups with respect to the operation (with or without tonsillectomy) is statistically significant ($P = 0.039$), but we count in the high failure group a very small number ($n = 8$). The median AHI postoperative for the successfully operated group was 11.5 (range 2-19), and for the unsuccessful (failures) operated group the median was 40.0 (range 20-69).

Discussion

Although many surgical techniques and (oral) devices have been propagated, UPPP is presently still the surgery of choice for OSAS and snoring. The actual success rate for the procedure in unselected patients is approximately 40%, and although this is disappointingly low, the results of several forms of alternative treatment are not much better, or these alternative treatment modalities have other severe disadvantages. With the aim to improve results of UPPP by means of better patient selection we in principal routinely perform sleep registration and sleep endoscopy in all patients with severe snoring or OSAS. Indeed we recently showed that this form of elaborate work-up is of worth, as our results of UPPP are better than historical controls in otherwise selected patients. However, we found in several patients a clear increase of AHI, while in others no change-was noted. In the patients with an increased AHI, with the exception of one, this was not due to a nasopharyngeal stenosis.

We were unable to find a clear correlation with variables such as age, gender, body mass index, earlier or concomitant tonsillectomy, unilevel (uvula-palate-tonsil) or multilevel (base of tongue as well) obstruction during sleep endoscopy and treatment outcome. A possible explanation for cure *versus* failure after UPPP seems to be unilevel or multilevel obstruction respectively.[12-15] Indeed, in series reporting on multilevel surgery better results were reported.[13-15] Riley *et al.*, carrying out multilevel surgery, concluded that pre-existing chronic obstructive lung disease, mandibular skeletal deficiency and obesity were the most significant factors in determining success or failure of treatment.[16] Cephalometric measurements for predicting the outcome of UPPP have been contradictory. Riley *et al.* found a correlation between the lowered position of the hyoid bone, the narrow airspace behind the tongue base and the success of UPPP.[17] Ryan *et al.* demonstrated that patients with a narrow airway tend to have good responses following UPPP.[18] Gislason *et al.*, however, found no correlation between these cephalometric measurements and results after UPPP.[19]

The outcome of UPPP is influenced by many factors. One of the most difficult factors in OSAS and its treatment is the diversity of obstructions and the fact that the obstruction is a dynamic process. Patients, to whom UPPP is offered, have to be informed that the treatment outcome can be improvement, no change or deterioration. The concept of three unrelated levels of obstruction, (a) nose-nasopharynx, (b) uvula-palate-tonsil and (c) base of tongue, seems therefore too static. Rather it seems that the soft palate and base of tongue have to be regarded as a dynamic functional entity, and that UPPP in some cases can lead to a too stiff palate, which in combination with an upward movement of the base of tongue can lead to increase of obstruction and narrowing of the upper airway. In this last outcome, adjuvant (surgical) treatment – such as hyoidthyroidpexia - can be indicated.

Conclusion

We conclude that although sleep endoscopy adds to better patient selection and better results, paradoxically, the finding of obstruction on palate-uvula level during sleep endoscopy does not guarantee a positive outcome of UPPP. More research into forms of topical diagnostic work ups and treatment of snoring and OSAS remains mandatory.

Acknowledgements

The authors thanks Mr. Guus Hart for his statistical advise and Dr. G. A. G. Davies for his linguistic assistance.

References

1. Fujita S, Conway W, Zorick F, Roth T. (1981) Surgical correction of anatomic abnormalities in obstructive sleep apnoea syndrome: uvulo-palatopharyngoplasty. *Otolaryngol Head Neck Surg* 89, 923-934.
2. Sher AE, Schechtman KB, Piccirillo JF. (1996) An American sleep disorders association review. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnoea syndrome. *Sleep* 19, 156-177.
3. Hessel NS, de Vries N. (2003) Results of uvulopalatopharyngoplasty after diagnostic work-up with polysomnography and sleep endoscopy; a report of 136 snoring patients. *Eur Arch Otorhinolaryngol* 260, 91-95.
4. Hessel NS, Laman MD, Ammers, VCPJ van, Duijn H van, Vries de N. (2002) Diagnostic work up of socially unacceptable snoring. Part I; History or sleep registration. *Eur Arch Otorhinolaryngol* 259, 154-157
5. Hessel NS, Vries de N. (2002) Diagnostic work up of socially unacceptable snoring: Part II; Sleep endoscopy. *Eur Arch Otorhinolaryngol* 259, 158-161.
6. Vincini C, Marani M, Frasconi PC. (1999) Failures in snoring and OSAS surgery. *Facial Plastic Surg* 15, 327-335.
7. Davis JA, Fine ED, Maniglia AJ. (1993) Uvulopalatopharyngoplasty for obstructive sleep apnea in adults: clinical correlation with polysomnographic results. *Ear Nose Throat J.* 72, 63-66.
8. Regestein QR, Ferber R, Johnson TS, Murawski BJ, Strome M. (1988) Relief of sleep apnea by revision of the adult upper airway. A review of clinical experience. *Arch.Otolaryngol.Head Neck Surg.*114, 1109-1113.
9. Zohar Y, Finkelstein Y, Talmi YP, Bar-Ilan Y. (1991) Uvulopalatopharyngoplasty: evaluation of postoperative complications, sequelae, and results. *Laryngoscope.*101, 775-779.
10. Krug P. (1999) Snoring and obstructive sleep apnea. *AORN J* 69, 792-801.
11. ASDA standards of practice (1997): The indications for polysomnography and related procedures. *Sleep* 20, 423-487.
12. Aboussouan LS, Golish JA, Wood BG, Mehta AC, Wood DE, Dinner DS. (1995) Dynamic pharyngoscopy in predicting outcome of uvulopalatopharyngoplasty for moderate and severe obstructive sleep apnea. *Chest.* 107, 946-951.
13. Petri N, Suadicani P, Wildschiodtz G, Bjorn-Jorgensen J. (1994) Predictive value of Muller maneuver, cephalometry and clinical features for the outcome of uvulopalatopharyngoplasty. Evaluation of predictive

factors using discriminant analysis in 30 sleep apnea patients. *Acta Otolaryngol.* 114, 565-571.
14. Riley,R, Guilleminault,C, Powell,N, Simmons,FB. (1985) Palatopharyngoplasty failure, cephalometric roentgenograms, and obstructive sleep apnea. *Otolaryngol.Head Neck Surg.* 93, 240-244.
15. Hendler BH, Costello BJ, Silverstein K, Yen D, Goldberg A. (2001) A protocol for uvulopalatopharyngoplasty, mortised genioplasty, and maxillomandibular advancement in patients with obstructive sleep apnea: an analysis of 40 cases. *J Oral Maxillofac Surg.* 59, 892-897.
16. Riley RW, Powell NB, Guilleminault C. (1989) Inferior mandibular osteotomy and hyoid myotomy suspension for obstructive sleep apnea: a review of 55 patients. *J Oral Maxillofac Surg* 47, 159-164.
17. Riley RW, Guilleminault C, Powell N, Simmons FB. (1985) Palatopharyngoplasty failure, Cephalometric roentgenograms and obstructive sleep apnea. *Otolaryngol.Head Neck Surg.* 93, 240-244.
18. Ryan CF, Dickson RI, Lowe AA, Blokmanis A, Fleetham JA. (1990) Upper airway measurements predict response to uvulopalatopharyngoplasty in obstructive sleep apnea. *Laryngoscope.* 100, 248-253.
19. Gislason T, Lindholm CE, Almqvist M et al. (1988) Uvulopalatopharyngoplasty in the sleep apnea syndrome. *Arch Otolaryngol Head Neck Surg.* 114, 45-51.

Table 1 **Summary of demographic and (pre-)operative data**

	Group I	Group II	Group III
Number	**32**	**15**	**8**
Female: Male	1: 31	2 : 13	1 : 7
Age			
Mean	47,8 ± 10,3 years	49,6 ± 7,9 years	46,9 ± 77 years
Range	23-69 years	36-63 years	36-58 years
BMI	28,5 ± 3.6 kg /m²	28,9 ± 2,5 kg /m²	28,8 ± 3,1 kg/m²
AHI			
Mean	26,5 ± 10,3 apnoeas/ h	26,7 ± 10,7 apnoeas/ h	48,12,6 ± 11,1
Median	24,0	25,0	48,0
Range	15-66	15-50	25-82
TE/ UPPP	25 (78 %)	9 (60%)	(38%)
UPPP	7 (22 %)	6 (40%)	5 (62 %)
Level(s) of Obstruction			
I, II	6 (19 %)	3 (20%)	1 (13%)
I,II,III	10(31 %)	5 (33 %)	3 (37%)
II	5 (16 %)	1 (7 %)	0
II,III	9 (28 %)	6 (40 %)	4 (50%)
X	2 (6 %)	0	0

Group I: responders after UPPP, with an AHI post-operative ≤ 20 and an AHI decrease of > 0 %
Group II: failures after UPPP, with an AHI increase of ≥ 0 %
Group III: failures after UPPP, with an AHI increase of ≥ 35 %
TE/ UPPP : tonsillectomy and UPPP peroperative.
Level(s) of obstruction I, nasal; II, oropharyngeal; III, hypopharyngeal; X, sleep endoscopy not performed

Chapter 7

SAMENVATTING, CONCLUSIE EN TOEKOMSTIGE ONTWIKKELINGEN

SAMENVATTING, CONCLUSIE EN TOEKOMSTIGE ONTWIKKELINGEN

In dit proefschrift worden enige recente ontwikkelingen in de diagnostiek en behandeling van sociaal onacceptabel snurken en licht tot matig ernstig obstructief slaapapneusyndroom (OSAS) behandeld. OSAS wordt gedefineerd door een aantal apnoes - totale obstructie van de bovenste luchtweg - en hypopnoes - partiële obstructie van de bovenste luchtweg - tijdens de slaap. De gouden standaard voor onderzoek naar OSAS is polysomnografie gedurende de gehele nacht, waarbij de ernst en het type van de slaapstoornis wordt vastgelegd. Er is geen consensus ten aanzien van de definitie van OSAS. In dit proefschrift is milde OSAS gedefinieerd bij een apnoe-hypopnoe index (AHI) tussen de 15 en 20 per uur, matige OSAS bij een AHI tussen de 20 en 30 en ernstige OSAS bij een AHI > 30. De diagnostiek en behandeling van sociaal onacceptabel snurken en obstructieve slaapapneu heeft de laatste twee decennia een stormachtige ontwikkeling doorgemaakt. De kennis over etiologie, morbiditeit, gezondheidsrisico's en diverse vormen van behandeling is enorm toegenomen. Er zijn veel verschillende benaderingen ten aanzien van diagnostiek en behandeling. Naast behandeling van algemene factoren zoals overgewicht, verkeerde slaaphouding, vermijden van gebruik van sedativa en alcohol, zijn ook lokale hulpmiddelen en ingrepen beschreven. Evenzeer is het inzicht in het belang van topische diagnostiek gestegen.

In het **eerste hoofdstuk** van dit proefschrift wordt een algemene inleiding en een historisch overzicht gegeven over snurken en obstructief slaapapneusyndroom. Hoewel in de literatuur al eeuwen fraaie beschrijvingen bestonden over de symptomatologie van snurken en slaapapneu is pas sinds circa twintig jaar duidelijk geworden hoe groot de impact voor de patiënt - in termen van morbiditeit en risico op langere termijn wat betreft tal van complicaties - en voor zijn partner is. Ook is duidelijk geworden dat het aandoeningen betreffen die zeer frequent voorkomen. Diverse diagnostische opties - om onderscheid te maken tussen sociaal onacceptabel snurken, OSAS en andere slaap gerelateerde ademhalingsstoornissen, evenals topische diagnostiek - en therapeutische opties worden beschreven.

In het **tweede hoofdstuk** wordt ingegaan op het belang van slaapregistratie. Hoewel er vragenlijsten ontwikkeld zijn die inzicht geven in de mate van slaperigheid overdag, zijn deze onvoldoende betrouwbaar gebleken om met voldoende zekerheid te kunnen voorspellen of sprake is van alleen sociaal onacceptabel snurken, of snurken als manifestatie van obstructief slaapapneusyndroom. Het beleid in het Sint Lucas Andreas Ziekenhuis in

Amsterdam is de laatste acht jaar geweest bij iedereen die zich meldt me sociaal onacceptabel snurken om een slaapregistratie te verrichten. Bij 54 % var onze patiënten bleek sprake van slaapapneu. Deze bevindingen sluiten aan bij de literatuur, waardoor de vraag geleidelijk aan verandert van bij wie eer slaapregistratie moet plaatsvinden, naar bij wie het niet moet gebeuren.

In het **derde hoofdstuk** worden de bevindingen van slaapendoscopie middels intraveneuze toediening van midazolam gepresenteerd. Goede topische diagnostiek is van belang indien een chirurgische ingreep overwogen wordt: is sprake van obstructie op uvula-palatum-tonsil niveau, op tongbasis–epiglottis-niveau, of op beide niveaus. De indruk bestond, dat onderzoek in zittende houding bij een wakkere patiënt geen goede afspiegeling zou kunnen zijn van obstructieniveaus tijdens slaap. Het onderzoek werd verricht bij patiënten in goede algehele conditie bij voorkeur met een apneu-hypopneu-index (AHI) lager dan - arbitrair – 30. Voor deze grens werd gekozen om twee redenen. Ten eerste achtten wij intraveneuze toediening van midazolam bij patiënten met een hogere AHI gevaarlijk, gezien de potentiële bijwerking -apneu - van midazolam. In de tweede plaats heeft bij patiënten met een AHI > 30, een behandeling met een overdrukmasker, - ook wel Nasal Continuous Positive Airway Pressure (NCPAP) - de voorkeur. In deze groep patienten is topische diagnostiek van minder belang. Inderdaad werden bij vele patiënten obstructies waargenomen, welke bij routine KNO-onderzoek niet verwacht werden. Ook bleek bij vele patiënten sprake van gemengde obstructie: zowel op uvula-palatum-tonsilniveau, als op tongbasisniveau.

Slaapendoscopie is in termen van kosten en tijd bewerkelijk en in **hoofdstuk vier** wordt een mogelijk alternatief, de akoestische flextube meting van obstructieniveaus tijdens slaapregistratie gegeven. De tube werd bij de patiënt ingebracht via de neus, waarna hij/zij de tube langzaam doorslikte. Een continue voor de patiënt niet waarneembaar geluid werd in de sonde gegenereerd en in de flextube voortgeleid. Bij een vernauwing van de flextube, werd het geluid gereflecteerd. De afstand tot de vernauwing, de duur en de ernst van de vernauwing werd door de apparatuur berekend. Hoewel de gedachte goed is, bleken de voorlopige ervaringen niet van dien aard dat dit onderzoek reeds een reëel alternatief voor slaapendoscopie is.

Gebaseerd op de bevindingen bij slaapregistratie en slaapendoscopie werd getracht een individueel bepaald behandelingadvies te geven. De uvulopalatop-haryngoplastiek (UPPP) is lange tijd - en waarschijnlijk nog - de meest uitgevoerde chirurgische ingreep voor sociaal onacceptabel snurken en lichte tot matig ernstige slaapapneu geweest. De ingreep is direct postoperatief belastend en pijnlijk, en meerdere andere ingrepen op palatinaal niveau zijn beschreven, maar deze hebben geen betere resultaten opgeleverd. De thans meest gebruikte definitie van succes van deze ingreep is een postoperatieve daling van apneu-index (AI, gemiddelde hoeveelheid ademstilstanden per uur) of apneu-hypopneu (reductie van ademstroom van 50%) index van minstens 50% en een reductie van AHI onder 20. Het succespercentage van de UPPP in grote meta-analyses blijkt in de orde van 40% te liggen. In **hoofdstuk vijf** worden de resultaten van UPPP, na slaapregistratie en slaapendoscopie gepresenteerd. UPPP werd verricht indien de voornaamste obstructie op palatinaal niveau gelokaliseerd was. De resultaten lagen in de orde van 70% succes, een belangrijke ondersteuning van de gedachte dat slaapendoscopie een wezenlijke bijdrage aan patiëntenselectie levert.

Verontrustend is dat bij meer dan 10% van de patiënten een negatief resultaat (toename van de AHI) gevonden werd. In **hoofdstuk zes** wordt op dit probleem ingegaan, en onderzocht werd of er duidelijke parameters zijn, op basis waarvan deze negatieve uitkomst te voorspellen is. In geval van multilevel obstructie (uvula-palatum en tongbasisniveau) was de kans op een goed resultaat van UPPP lager dan indien alleen obstructie op uvulapalatumniveau werd gezien. Ook bij patiënten die eerder tonsillectomie hadden ondergaan, was het effect minder goed dan als de tonsillen gelijktijdig met de UPPP werden verwijderd. De *body mass index* (BMI) was iets hoger in de patiëntengroep met slecht resultaat.

De ervaringen in dit proefschrift gepresenteerd zullen hopelijk bijdragen tot verder onderzoek naar diagnostiek en behandeling van sociaal onacceptabel snurken en lichte tot matig ernstige slaapapneu en leiden tot optimale behandelingsresultaten met zo weinig mogelijk morbiditeit. Het onderwerp is volop in beweging, en vele verschillende niet operatieve oplossingen, niet chirurgische invasieve interventies en chirurgische mogelijkheden zijn mogelijk.

Wat betreft de toekomstige ontwikkelingen denken we, dat ondanks de uitvoerige diagnostiek en patiëntenselektie, zoals beschreven in dit proefschrift, met duidelijk betere resultaten van UPPP in vergelijking met andere studies, UPPP niet verder te optimaliseren is. UPPP zal een rol blijven spelen in de chirurgische behandeling van sociaal onacceptabel snurken en licht tot matig obstructief slaap apneu syndroom, maar het lijkt onwaarschijnlijk dat verdere chirurgische modificaties zullen leiden tot een (bijna) 100% succespercentage. Chirurgische behandeling ontwikkelt zich meer in de richting van een meer anatomisch gerichte benadering. Verdere verbetering valt te verwachten van andere technieken en succespercentages van deze technieken moeten worden vergeleken met die van de UPPP. Van alle nieuwe behandelingen zulllen de indicaties, contra-indicaties en beperkingen, voor- en nadelen, succespercentages,

morbiditeit en complicaties moeten worden vastgesteld. Dit geldt voor (combinaties van) radiofrequente thermotherapie van de concha inferior, palatum molle en tongbasis, hyoidthyroidpexie en de uitgebreide maxillofaciale ingrepen. Niet invasieve behandelingen (*oral devices* en NCPAP) zullen een belangrijke rol behouden. Idealiter zal de behandelend specialist moeten kunnen beschikken over de diverse behandelingsopties en een individueel behandelingsadvies aan de patiënt moeten geven.

SUMMARY, CONCLUSIONS AND FUTURE DEVELOPMENTS

SUMMARY, CONCLUSIONS AND FUTURE DEVELOPMENTS

This thesis deals with some recent developments in the diagnostic workup and treatment of socially unacceptable snoring and mild to moderate obstructive sleep apnea (OSAS). OSAS is defined by a number of apneas – total obstruction of the upper airway- and hypopneas- partial obstruction of the upper airway during sleep. The gold standard investigation for OSAS is full night polysomnography from which the type and severity may be detected. There is no consensus on the definition of OSAS. In this thesis, mild OSAS is established by an AHI between 15-20 per hour, moderate OSAS by an AHI of 20-30, and severe OSAS by an AHI > 30. The diagnostic workup and treatment of socially unacceptable snoring and obstructive sleep apnea have been subject to a tremendous development in the past two decades. The knowledge about aetiology, morbidity, health risk and various forms of treatment has increased considerably. Various approaches to diagnosis and treatment exist. In addition to treatment of general factors such as obesity, sleeping position, avoidance of sedatives and alcohol, local interventions and surgical treatments have been developed. The insight in the importance of topical diagnostic workup in order to offer side-specific treatment has increased as well.

In **Chapter one** of this thesis, a general introduction and historical overview on snoring and obstructive sleep apnea is presented. Although in the literature already centuries ago adequate descriptions on symptomatology of snoring and sleep apnea have appeared, it has only since the past two decades become clear how big the impact for the patient - in terms of morbidity and risk for various complications – and for the partner is. It has also become clear that snoring and sleep apnea are frequently occurring problems. A variety of diagnostic options- to distinguish between socially unacceptable snoring, OSAS and other sleep related breathing disorders, as well as topical differentiation- and therapeutic options is presented.

In **Chapter two** the importance of sleep registration is stressed. Although questionnaires have been developed that deal with sleepiness during daytime, these have been shown to be not sufficiently reliable to predict if a patient is only a socially unacceptable snorer, or snores as manifestation of obstructive sleep apnea. The policy at the Saint Lucas Andreas Hospital in Amsterdam, the Netherlands, in the last 8 years has been to perform sleep registration in all cases of socially unacceptable snoring. In 54 % of all patients, obstructive sleep apnea was found. These findings are in agreement with the literature. Gradually the question is changing to who should have sleepregistration to who should not have it.

In **Chapter three** the findings of sleep endoscopy by means of intravenous application of Midazolam are presented. Good topical diagnostic workup is of importance if a surgical treatment is considered: is the obstruction localised on uvula-palate-tonsillair level, at the level of base of tongue/epiglottis, or both. We believe that routine ENT examination, in the sitting position, in an awake patient, is not a reliable reflection of level(s) of obstruction during sleep. The investigation was performed in patients in otherwise good condition, with an apnea-hypopnea-index (AHI) < than 30. This cut-off point was chosen for two reasons. Firstly the intravenous application of Midazolam in patients with a higher AHI is potentially dangerous, since apnea is a known side effect of Midazolam. Secondly, treatment with Nasal Continuous Positive Airway Pressure (NCPAP) will be offered to patients with an AHI > 30 as treatment of choice. In these patients topical diagnosis is of lesser importance. We indeed found in many patients levels of obstruction(s), that where not expected based on the findings by routine ENT-examination. In many patients multilevel obstruction was found: both on uvula-palate-tonsillar level, as well as on base-of-tongue level.

Sleep endoscopy in terms of costs, time and burden for the patient has downsides as well. In **Chapter four** a possible alternative, the acoustic flextube Rhinosleep which analysis levels of obstruction during sleepregistration, is presented. The tube was inserted through the nose and slowly swallowed by the patient. A continuous white band noise was generated in the probe and sent into the flextube. When the flextube was narrowed the noise was reflexted. The distance to the narrowing and the duration and degree of the narrowing were calculated by the measuring system. The preliminary experience shows that Rhinosleep is not yet a viable alternative for sleependoscopy for several practical reasons.

Based on the findings with sleep registration and sleep endoscopy an individually tailored treatment advice is given. The uvulopalatopharyngoplasty (UPPP) has been - and still is - the workhorse of surgical treatment of snoring and mild to moderate obstructive sleep apnea. The procedure is painful immediately postoperatively, it has considerable side-effects and a moderate success rate. Various other forms of surgical treatment on palatal level have been described, albeit not with better results. The most often used definition of success of this treatment is a postoperative decrease of apnea-index (AI, mean number of apneas per hour) or apnea-hypopnea (reduction of airflow of > 50%) index of at least 50% and a reduction of AHI under 20. The succesrates of UPPP in meta-analyses are approximately 40 %.

In **Chapter five** our results of UPPP, after sleepregistration and sleependoscopy are presented. UPPP was performed when the main level of obstruction was at the palatal level. Our results were in the order of 70% success, which supports our policy to use sleep endoscopy as an important diagnostic procedure to select suitable patients.

We were unpleasantly surprised to find that > 10% of the patients had a negative effect (increase of AHI). In **Chapter six** this problem is dealt with. We analysed various parameters to see whether negative treatment outcome could be predicted. A negative trend was apparent for multilevel obstruction, previous tonsillectomy, and for higher than average body mass index (BMI).

The experiences presented in this thesis will hopefully lead to further research into diagnostic workup and treatment of patients with socially unacceptable snoring and mild to moderate sleep apnea and help to establish optimal treatment results with as little morbidity as possible.

In terms of future developments we believe that, although the work up and patient selection described in this thesis, undoubtedly leads to better results of UPPP as compared to historical controls, UPPP has reached its limitations.

UPPP will continue to play a role in the surgical treatment of socially unaccept-able snoring, and mild to moderate obstructive sleep apnea, but it is unlikely that further surgical modifications will lead to a (near) 100% success rate. Surgical treatment is developing into a more site-specific approach. Further improvements in the treatment of socially unacceptable snoring and obstructive sleep apnea will come from other techniques, and success rates of these techniques have to be compared with those of UPPP. Of all new treatment options, indications, contra-indications and limitations, upsides and downsides, success rates, morbidity and complications have to be defined. Such techniques include (combinations of), radiofrequent thermotherapy of inferior turbinates, soft palate and base of tongue, hyoidthyroidpexia and more extensive maxillofacial interventions. Non invasive treatment (oral devices and NCPAP) will continue to play an important role as well. Ideally the responsible physician should have access to all different treatment options and should give an individually tailored treatment advice to the patient.

Chapter 9

List of publications

List of publications

N.S. Hessel, D.M. Laman, V.C.P.J. van Ammers, N. de Vries, H. van Duijn (2000) Sleependoscopy with artificial induction of sleep and somnography in 385 snorers. *Sleep-wake Research in the Netherlands* (A.L. van Bemmel, D.G.M. Beersma, H. Folgering, W.F. Hofman, G.S.F. Ruigt, (eds.) Volume 11, pp 68-72.

N.S. Hessel, D.M. Laman, V.C.P.J. van Ammers, H. van Duijn, N. de Vries (2001) Hebben apneu- en hypersomnolentie klachten een voorspellende waarde voor de uitkomst van slaapregistratie bij patiënten die sociaal onacceptabel snurken? (verenigingsverslagen) *Ned Tijdschr Geneeskd* 145 (22): 1096.

N.S. Hessel, D.M. Laman, V.C.P.J. van Ammers, H. van Duijn, N. de Vries (2002) Diagnostic work up of socially unacceptable snoring. Part I; History or sleep registration. *Eur Arch Otorhinolaryngol* 259:154-157.

N.S. Hessel, N. de Vries (2002) Diagnostic work up of socially unacceptable snoring. Part II; Sleep endoscopy. *Eur Arch Otorhinolaryngol* 259:158-161.

N.S. Hessel, N. de Vries (2003) Results of uvulopalatopharyngoplasty after diagnostic work-up with polysomnography and sleep endoscopy; a report of 136 snoring patients. *Eur Arch Otorhinolaryngol* 260:91-5.

N.S. Hessel, D.M. Laman, V.C.P.J. van Ammers, H. van Duijn, N. de Vries (2003) Feasibility study of Flextube reflectometry for localisation of upper airway obstructions for obstructive sleep apnea. *Rhinology* 41:87-90.

C. den Herder, N.S. Hessel, N. de Vries (2004) Hyoidthyroidpexie, een nieuwe behandeling voor obstructief slaapapneusyndroom. *Ned Tijdschr KNO-Heelk* 10:25-29.

N.S. Hessel, N. de Vries. Increase of the apnoea-hypopnoea index after uvulopalatopharyngoplasty: analysis of failure. Accepted for publication: Clin Otolaryngol

N. de Vries, C den Herder, N.S. Hessel (2004) Behandeling van het obstructieve slaapapneusyndroom bij volwassenen. *Ned Tijdschr Geneeskd* 148:250-1.

Chapter 10

Dankwoord

Dankwoord

Tot slot wil ik iedereen bedanken die een bijdrage aan de totstandkoming van dit proefschrift hebben geleverd:

Dr. N. de Vries. Nico, allereerst wil ik jou bedanken. Door jou werd de stap van 'wat onderzoek doen tijdens de co-schappen' naar een promotieonderzoek een logische en zinvolle keuze. Ondanks je vele verantwoordelijkheden in allerlei functies en een overvolle agenda, heb je de gave om niet alleen mij, maar ook andere jonge onderzoekers, te stimuleren en te begeleiden naar publicaties en uiteindelijk een proefschrift. Je maakt toch elke keer tijd vrij voor datgene wat je ook echt leuk vindt, namelijk het onderzoek. Ik heb veel respect voor je analytische manier van denken, heldere schrijftaal en politieke aanpak. Je 'overview', toegankelijkheid en levensgenieterinstelling roepen veel bewondering bij me op. Tevens blijkt de combinatie van klinisch werk en onderzoek tijdens mijn periode in het Sint Lucas Andreas Ziekenhuis een bijzonder leerzame en vooral prettige en unieke manier van werken te zijn, waar ik natuurlijk jou en je partner, dr. Peter van Rijn, KNO-arts, in het bijzonder dankbaar voor ben. Dit hebben we in iedergeval voor elkaar gekregen. Veel dank daarvoor.

Prof.dr. C. R. Leemans. Beste René, ik ben je uiterst dankbaar voor je waardevolle suggesties, kritiek en het feit dat ik onder jou mag promoveren. Je frisse en deskundige blik is van grote betekenis voor mijn proefschrift.

Prof.dr. G. B. Snow, Prof.dr. J. J. Manni, dr. R. M. L. Poublon, Prof.dr. P. van de Heyning, Prof.dr. P. E. Postmus, Prof.dr. C. J. Stam. Ik ben u zeer erkentelijk voor de tijd die u heeft besteed aan mijn manuscript, de opbouwende kritiek aangaande dit proefschrift en de invulling daarvan in de vorm van zitting nemen in de oppositiecommissie tijdens de verdediging van mijn proefschrift.

Verschillende onderzoeken beschreven in dit proefschrift zijn tot standgekomen in samenwerking met de afdeling Klinische Neurofysiologie van het Sint Lucas Andreas Ziekenhuis. Mijn dank gaat uit naar een ieder die hier werkzaam is en vol enthousiasme tijd vrij maakte, zodat er snel 'zaken' gedaan kon worden. Natuurlijk zal ik de uiterst deskundige visie, wijze raad en vriendelijke woorden van *dr. Hans van Duin,* klinisch neurofysioloog niet vergeten. Evenals het onmetelijke enthousiasme en de kritische blik van *drs. Martin Laman,* klinisch neurofysioloog. En natuurlijk de man waar ik de meeste uurtjes voor berekeningen en het bedenken van handige strategieën mee heb doorgebracht, *Vincent van Ammers.* Vincent, je bent uniek.

Binnen het instituut Sint Lucas Andreas Ziekenhuis heb ik met bewondering de effectieve en bereidwillige medewerking ervaren van mensen die het geheel gesmeerd deed verlopen. *Hans Moinat,* 'de fotograaf', jij bent op heel wat 'last minute' momenten, voor diverse presentaties een rots in de branding geweest. Met fietskleren voor de terugweg naar huis al aan, kon ik toch nog snel bij je terecht. En natuurlijk *Marianne van Wegen,* medisch bibliothecaresse, zonder jouw hulp vraag ik me af of alle literatuur wel goed bij te houden was geweest. *Dr. G.A.G. Davies,* radioloog en Bourgondiër in hart en nieren, ben ik voor de kritische rode stift, ter correctie van mijn engelse publicaties, en dat alles voor een goede fles wijn, meer dan erkentelijk. En dan natuurlijk de *doktersassistenten,* die altijd met oprechte interesse informeren hoe het onderzoek verliep en die het leven lekker luchtig en gezellig maakten. 'Massages' ter ontspanning en attenties op momenten dat je ze niet verwachtte. Jullie zijn schatten.

De heer *Guus Hart,* statisticus, werkzaam in het Antoni van Leeuwenhoekhuis en het Academisch Medisch Centrum Amsterdam ben ik zeer dankbaar voor de bijdrage aan de analyses van verschillende onderzoeken in mijn proefschrift.

Ed Spall en *Ben Schoonhein,* mannen, jullie zijn toppers in vakkundigheid, snelheid en geduld. De tijdsdruk was voor jullie een uitdaging. Geniet, want het is mede dankzij jullie gelukt.

Paulo Kalmijn, ik bewonder je om je enorme mensenkennis en je analyses. Door jou wordt het promoveren mede een feit. Enorm veel dank hiervoor.

Mijn paranimfen, *Clara* en *Nickie,* wat een fijn idee dat jullie deze zware taak willen accepteren en dat allemaal voor mij... Nick, toch nog een keer paranimf, terwijl je dacht de laatste in de rij der promovendi te zijn geweest en helaas geen gekke grappen en grollen meer op zo`n belangrijk moment te kunnen uithalen. Ik waarschuw je! Je bent echt een enorme relativeerder en nuchtere vriend met ongelooflijk veel humor, dank hiervoor. En dan Clara, de rots in de branding, met altijd een luisterend oor, waarna vaak wijze raad en je gaat geen uitdaging uit de weg, zo ook niet jouw zware taak als paranimf. Ik hoop dat er nog vele vriendschapsjaren volgen.

Mijn vrienden, die allen zo begaan zijn met de afronding van deze taak. *Danielle,* gaan we de afronding vieren met een weekendje skeeleren op Texel? *Jörn,* of jouw-sponsortips vruchten afwerpen, weet ik nu nog niet, maar je zult het aan het diner wel merken. *Koen* en *Trudy,* wat een toeval en geluk dat we allen vier jaar geleden zo nodig Indonesië wilden verkennen (en Koen zijn mobieltje mee had genomen). Jullie zijn kanjers. Jurgen, wat moest ik zonder jou en laptop beginnen? Dank voor je jarenlange vriendschap, mensen- en computerkennis. *Mo, Evelien, Bram, Claudia, Armando, Patrick, Manouck,* wel eens een keer een afspraak verzetten, vanwege het promotie onderzoek, is een understatement. Dank voor jullie begrip en vriendschap. Mijn neef en goede vriend, *Jeroen,* 'als ik wat voor je kan doen..?'. Dank je. Mijn tennisvriendinnen en vrienden, *Nathalie, Frederiek, Sanne, Mariëlle* en *Jan,* wat een zaligheid om even tussen het werk door, gezamenlijk de tegenstanders in te maken. Althans, collectief dat voornemen te hebben. Dit jaar gaan we het gewoon doen! De *Salsavrienden.* Fijn dat jullie altijd even enthousiast zijn om me weer te zien en te dansen, zelfs na maandenlange afwezigheid, vanwege het werk.

Tineke en *Richard,* we gaan de afronding zeker vieren! Dank voor jullie vertrouwen en altijd oprechte enthousiasme.

Alle stafartsen, mijn collega arts-assistenten, secretariaat-medewerkers en kliniek- en poliverpleegkundigen en verplegers. Hartelijk dank voor jullie begrip, geduld, hulp en belangstelling voor deze promotie.

Mijn zus *Gabriëlle* en *Jeffrey,* met jullie goede hart en steun is de klus toch geklaard. Dank jullie voor het onvoorwaardelijke vertrouwen.

Tot slot wil ik mijn ouders de terechte eer van rijensluiter in mijn dankbetuiging geven. Met jullie liefde, vertrouwen en onbeschrijflijke hulp in vele vormen, hebben jullie mij de basis gegeven, waardoor het onmogelijke, mogelijk wordt. Bedankt voor alles.

Chapter 11

Curriculum vitae

Curriculum vitae

Natascha Serena Hessel werd op 1 augustus 1970 geboren in Breda. Vanaf haar 16e jaar heeft zij enkele jaren in Duitsland met haar familie gewoond. In 1991 behaalde zij haar VWO diploma aan het Graafschapcollege te Doetinchem. Het jaar hierna heeft zij gewerkt, de wereld rondgereisd en haar natuurkunde toelatingsexamen te Utrecht behaald.
In 1992 begon ze haar studie geneeskunde aan de Universiteit van Amsterdam, die ze in 2000 afrondde. Tijdens de co-schappen fase startte Natascha met onderzoek bij dr. N. de Vries aan de afdeling Keel-, Neus- en Oorheelkunde in het Sint Lucas Andreas ziekenhuis te Amsterdam (1998-2000). Op 28 juni 2000 behaalde zij haar artsexamen aan de Universiteit van Amsterdam.
Van 1 juli 2000 tot 1 november 2002 werkte zij als arts-assistent aan de afdeling Keel-, Neus- en Oorheelkunde in het Sint Lucas Andreas ziekenhuis te Amsterdam, waar tevens het onderzoek werd voortgezet.
Per 1 november 2002 startte zij als arts-assistent aan de Keel-, Neus- en Oorheelkunde afdeling van het VU medisch centrum onder leiding van Prof.dr. C.R. Leemans, om op 1 maart 2003 met de opleiding tot KNO-arts te beginnen.