Developments in Diagnosis and Treatment of Obstructive Sleep Apnea Syndrome

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Developments in Diagnosis and Treatment of Obstructive Sleep Apnea Syndrome

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chapter 1

GENERAL INTRODUCTION

1.1 History

The term “Pickwickian” was first used by Sir William Osler (1849-1919), to describe patients who were both obese and hypersomnolent. Obviously, Osler was a reader of Charles Dickens as the Dickens novel *The Posthumous papers of the Pickwick club,* published in 1837, had a character in it that was similar to the patients he had identified with these common symptoms. [Dickens, 1837] Osler noted in the fourth edition of his *The Principles and Practice of Medicine,* published in 1901, that “an extraordinary phenomenon seen occasionally in excessively fat young persons is an uncontrollable tendency to sleep.”[Osler, 1901] In the sixth edition, published in 1905, he added the phrase “like the fat boy in *Pickwick*.”[Osler, 1905]

In 1956 Charles Sidney Burwell described patients who were obese and suffered from extreme sleepiness or fatigue, twitching, cyanosis, periodic respiration, polycythemia, right ventricular hypertrophy, and right ventricular failure. He termed these patients people with Pickwickian Syndrome.[Burwell, 1956]

In 1965 Henri Gastaut started doing research on what is now called Obstructive Sleep Apnea Syndrome (OSAS). He recorded breathing and sleeping patterns of a patient with Pickwickian Syndrome and discovered distinctive patterns of the 3 types of apnea.[Gastaut, 1965]

From 1969 OSAS was often treated with a tracheostomy; bypassing the upper air passage altogether by creating an incision or opening in the trachea and inserting a cannula.[Kuhlo, 1969]

In 1981, an Australian researcher by the name of Colin Sullivan, published his findings on the treatment of OSAS with a so-called nasal Continuous Positive Airway Pressure machine, or nCPAP.[Sullivan, 1981] The treatment plan started off with a reversed vacuum cleaner motor that blew air into the nasal passage using a Silastic tube to keep the airway open. The initial CPAP machines were large, bulky and noisy.

After these initial therapies, the last three decades have seen many improvements made and new therapeutic options introduced. But, as you will find out in this thesis, there is still much work to be done.

1.2 Prevalence

On the basis of the criteria of the American Academy of Sleep Medicine (AASM) [AASM,1999] the prevalence of OSAS in Dutch general practice is 0,45% among males of 35 and older. [Knuistingh Neven, 1998] Among American employees of between 30 and 60 years of age the prevalence is calculated at 4% for men and 2% for women. [Young, 1993] It is estimated that at least 80% of OSAS patients has not been diagnosed yet.[Young, 1997]

1.3 Definitions

In recommendations of the AASM published in 1999 OSAS has been defined as an affliction with complaints of excessive sleepiness during the day combined with respiratory events of the obstructive or mixed type determined by means of polysomnography, which complaints cannot be explained by other causes. Patients with suspected OSAS have to meet the following criteria A or B, combined with C.

A: excessive sleepiness during the day, which cannot be explained in any other way
B: two or more of the following complaints which cannot be explained in any other way:
- interrupted breathing
- repeatedly waking up with a start
- not feeling refreshed after sleep
- feeling tired during the day
- loss of concentration

C: more than five obstructive respiratory events per hour of sleep at night

The severity of OSAS is determined on the basis of the mean number of obstructive respiratory events per hour of sleep at night. This is called the apnea-hypopnea index (AHI). An AHI of 5-15 is called mild OSAS, 15-30 moderate OSAS and 30 or more severe OSAS.[AASM, 1999]

1.4 Sleepiness

Hypersomnolence during the day is the most important complaint of OSAS patients and partly determines therapeutic policy. It is therefore necessary to be aware of the various other causes of hypersomnolence. Applying differential diagnostics, the following have to be considered: lack of sleep, sleeplessness, periodic limb movement syndrome (PMLS),

narcolepsia, idiopathic hypersomnia, hypoventilation, medication, hyperventilation, panic disorder, and other mental or physical complaints.

To measure sleepiness, questionnaires and tests have been developed. The questionnaire most often used is the Epworth Sleepiness Scale (ESS) (table 1).[Johns, 1991] This questionnaire quantifies the tendency to fall asleep during different activities. An ESS>10 is regarded as deviant. The ESS provides an easy first impression of the patient's tendency to fall asleep. Unfortunately, the reproducibility of the ESS is considerably smaller than originally assumed. [Nguyen, 2006] Examples of objective tests to quantify sleepiness are tests that measure reaction speed (Osler test), the capacity to stay awake (maintenance of wakefulness test, MWT), or, alternatively, the capacity to fall asleep (multiple sleep latency test, MSLT).[Littner, 2005]

Table 1 ESS

Situation	**Score***			
While sitting or reading	0	1	2	3
While watching television	0	1	2	3
Outside the home, in a meeting, at the cinema or a pub	0	1	2	3
During a one-hour car journey as a passenger	0	1	2	3
Lying quietly in circumstances admitting sleep	0	1	2	3
While visiting or while having a conversation with someone	0	1	2	3
Following a hot meal	0	1	2	3
When driving while waiting for traffic lights or in a queue	0	1	2	3
Total score				

**0 = I would never doze off*
1 = I would occasionally doze off
2 = I would doze off pretty regularly
3 = I would always doze off

1.5 Polysomnography

Polysomnography consists of multiple tests to monitor different aspects of sleep. Electroencephalogram, electrooculogram and submental electromyogram record sleep pattern. Thoracoabdominal excursions are registered by straps containing piezoelectric transducers to monitor breathing effort. Apneas and hypopneas are recorded by measuring nasal airflow with a pressure sensor. Pulse oximetry is used to monitor oxygen saturation (SaO_2) and heart rate. In addition, ECG, movements of the limbs, the intensity of snoring and sleep position are recorded.

In the Sint Lucas Andreas Hospital electrodes and sensors are placed and equipment is calibrated in the late afternoon. The system is switched on and off at 7.00 p.m. and 7.00 a.m. respectively. All signals are recorded with DDD (digital sampling, digital filtering, digital storage) recording technology. Storage is done on a PCMCIA flash-card. The following day, the data is downloaded to the computer and analyzed by dedicated sleep software and manually reviewed by an experienced sleep investigator for final analysis.

An apnea is defined as a pause in breathing of 10 seconds or more. During an obstructive apnea there is a continuous or progressive effort to breathe. During a central apnea there is no effort to breathe whatsoever. A mixed apnea begins as a central apnea and ends as an obstructive apnea. A hypopnea is an airflow reduction of more than 30% lasting 10 seconds or more, combined with a drop in saturation of more than 4%. A Respiratory Effort Related Arousal (RERA) is by definition an obstructive event of 10 seconds or more, but does not completely meet the criteria for apnea or hypopnea. It is characterized by a very slight change in airflow or respiratory effort terminated by an EEG arousal and there is no drop in saturation.

1.6 Pathophysiology

The respiratory neurons controlling the regular inspiration and expiration are located in the pons and medulla oblongata of the brainstem. There is not one clearly defined breathing centre but a network of respiratory neurons. These neurons control the exact timing in activating the muscles of the upper and lower airways and the accessory breathing muscles. Activation of the respiratory muscles causes intrathoracal negative pressure and ultimately inspiration of air. A decrease in the activation of the respiratory muscles results in an increase of the intrathoracal pressure which in turn causes expiration. Part of the neuronal control of respiration is the lung inflation reflex. This reflex occurs in response to the pulmonary stretch receptors. When the lungs are stretched more, the afferent neurons of the nervus vagus increase their activity. This interrupts inhalation and starts off expiration and vice versa. The periodic activity of the respiratory network is dependent on a non-rhythmic, tonic activation by afferents from the reticular formation of the brainstem.

Sleep influences this tonic activity. A drop in sensory input causes the reticular activity of the brainstem to decrease, especially during NREM sleep. Furthermore, particularly during REM sleep, the muscle tone of both the motor system and the respiratory muscles drops, with the exception of the diaphragm. Moreover, the arousal threshold as well as the thresholds of the hypoxic and hypercapnic respiratory drives are higher at night and vary during the night and per sleep stage.

Main factors influencing decrease in cross-sectional diameter of the upper airway include increased external pressure (obesity) and constrictor activity, decreased dilator activity and hypoxic muscle fatigue. The above physiological changes during sleep combined with these factors ultimately cause OSAS. [Hörmann, 2006]

1.7 Consequences

1.7.1 Symptoms

Main symptoms of sleep apnea are: intermittent sleepiness during the day, snoring, and diminished intellectual achievements. Other symptoms are personality changes, headaches in the morning, and enuresis nocturna.

1.7.2 Traffic accidents

It appears that patients with OSAS run an increased risk of being involved in road accidents. It is argued that drivers with OSAS are involved in road accidents 3 to 10 times as often as other drivers.[Connor, 2001; Horstmann 2000; Lloberes, 2000; Howard, 2004; Young, 1997] In the Netherlands the ministerial rules concerning driving and OSAS were revised in 2008. The rules distinguish between driving passenger cars and motorbikes on the one hand and driving lorries and buses on the other hand. It is advised that all drivers with OSAS are treated adequately for at least two and three consecutive months respectively, which implies that their AHI must be below 15. This is to be judged by a lung specialist or a neurologist who is not the patient's doctor. For the evaluation the same instruments must be used as are used in diagnosing. Initially the driving licence will be valid for one year, thereafter validity will be three years for passenger cars and motorbikes and one year for lorries and buses. Doctors are not yet obliged to report patients with OSAS. However, the doctor should be instructing them that they are not allowed to drive motor vehicles on the open road until they meet the current criteria.[Stigter, 2009]

1.7.3 Long-term consequences

Whether OSAS is a risk factor for cardiovascular diseases has always been difficult to determine on account of the many "confounding factors" in OSAS patients.[Kiely, 2000; Bauget, 2005] There is, for instance, a clear connection between OSAS and obesity. The average OSAS patient is overweight and hypertension and metabolic disorders like glucose intolerance are common among OSAS patients. Yet, the number of indications that OSAS is a cardiovascular risk factor has steadily grown over the years.[Buyse, 2007; McNicholas, 2007; Caples, 2007] In particular those studies in which treatment of OSAS with nCPAP is examined show a decrease of

cardiovascular risk.[He, 1988; Veale, 2000; Marti, 2002; Marin, 2005] There is no conclusive scientific evidence that OSAS forms an independent risk factor for cardiovascular diseases. [Buyse, 2007; McNicholas, 2007] The heightened risk may be the result of various different riskfactors.

Increased sympatic acivity

Severe OSAS patients show heightened levels of plasma and urine catecholamines with normalisation after nCPAP therapy.[Heitmann, 2004]

Endothelial dysfunction

The endothelium of the vascular wall uses vasoactive mediators to control the balance between vasodilatation and vasoconstriction. Endothelial dysfunction is a shift in the balance towards vasoconstriction and is regarded as a preliminary stage of atherosclerosis. This dysfunction also occurs with well known cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia and smoking. Nitric Oxide (NO) is the best known vasoactive mediator. In OSAS patients NO turns out to be produced in smaller quantities or to be less active. In normotensive OSAS patients nCPAP treatment raises NO activity [Ip, 2000] and brings about a normalisation of the endothelial balance.[Philips, 1999]

Oxidative stress

Intermittent hypoxaemia which occurs with OSAS seems responsible for diminished NO availability. This could link oxidative stress in OSAS patients with endothelial dysfunction. [Lavie, 2004]

Inflammation

Systemic inflammation occurs in response to local processes in the atherosclerotic vascular wall. Markers which are heightened in this systemic inflammation, like CRP, TNF-α, IL-8 and HIF-1 gene, have also been identified in OSAS patients. It has been documented that as a result of nCPAP therapy some of these markers, CRP and TNF-α, are diminished.[McNicholas, 2007]

Metabolic dysfunction

Glucose intolerance, in particular insulin resistance, occurs with OSAS patients independent of their body weight.[Punjabi, 2005; Spiegel, 2005] Epidemiological studies show that diabetes mellitus is strongly associated with OSAS. [Meslier, 2003] The intermittent hypoxaemia is thought to induce glucose intolerance.[Oltmanns, 2004] The degree of insulin resistance seems to be dependent on the level of the AHI, corrected for weight.[Punjabi, 2002]

1.8 Physical examination

1.8.1 Examination of the upper airway

In OSAS patients the entire upper airway is to be examined thoroughly. The cause of the condition may be found at any point in the upper airway, from nose to larynx. Common causes of obstruction in the nose are septal deviation, turbinate hypertrophy, nasal polyps, valve insufficiency, and swelling of the mucous membrane.

Causes in the nasopharynx may be adenoid hypertrophy, but also obstructive benign or malignant tumors.

The most important area of examination are the mouth and oropharynx. The length of the palate and the uvula, the size of the tonsils and the size of the tongue must be examined carefully. Grading systems have been devised for both tonsil size and tongue size. Tonsil size may be expressed in five grades (table 2). The Modified Mallampati Score, developed by Friedman, is a score to grade tongue size (table 3). Friedman combined the two grading systems into the Friedman Staging System (table 4). With this he tried to assess the level of obstruction and to identify prognostic indicators for the chance of success of a particular operation. Patients scoring a low grade of the Friedman staging system would have a higher change to success with a uvulopalatopharyngoplasty with/without tonsillectomy than patients scoring a high grade.[Friedman, 2002, 2004]

Table 2 Tonsil size

Tonsil size	Grade
Previous tonsillectomy	0
Tonsils hidden within the tonsillar pillars	1
Tonsils extending to the tonsillar pillars	2
Tonsils extending beyond the tonsillar pillars	3
Tonsils enlarged and extending to the midline; “kissing tonsils”	4

Table 3 Tongue size

Tongue size	Grade
Uvula, tonsils, soft and hard palate visible	I
Uvula and tonsils partly visible, soft and hard palate wholly visible	II
Uvula not visible, soft and hard palate visible	III
Only hard palate visible	IV

Table 4 Friedman staging system

Situation	Stage
Tonsil size: 3-4, Tongue size: 1-2	I
Tonsil size: 0-1-2, Tongue size: 1-2 Tonsil size: 3-4, Tongue size: 3-4	II
Tonsil size: 0-1-2, Tongue size: 3-4	III
Patients with BMI>40 and/or craniofacial abnormalities (like retrognathism)	IV

It is also important to carefully examine the lowest point of the upper airway, the larynx, for causes of airway obstruction. The dental status, position of the jaws, neck circumference and BMI must also be part of the examination.

1.8.2 Sleep endoscopy

With sleep endoscopy it is possible to perform a dynamic assessment of the upper airway from the nose to the larynx during sleep. It is done under sedation with midazolam or propofol using a flexible endoscope. In this way it is possible to get an idea of the level and extent of obstruction and also what happens when the mandible is advanced during sleep. The main respiratory parameters, AHI and mean SaO_2, do not significantly change with benzodiazepines or propofol sedation, however sleep architecture does.[Sadaoka, 1996; Rabelo, 2010] While performing sleep endoscopy the anesthetic depth is of main importance. Decrease in genioglossus tone and increase in pharyngeal critical closing pressure exist proximate to loss of consciousness. This suggests an particular vulnerability at the transition from conscious to unconscious sedation.[Hillman, 2009] Berry et al. validated sleep endoscopy by performing it in a group of symptomatic and a group of asymptomatic individuals. None of the asymptomatic group snored or obstructed during the procedure entirely unlike the symptomatic group.[Berry, 2005] The interrater reliability of drug-induced sleep endoscopy is moderate to substantial. [Kezirian, 2010] The test-retest reliability appears to be good.[Rodriguez-Bruno, 2009] A few studies have examined the association between sleep endoscopy findings and outcomes of palate surgery and mandibular repositioning appliances.[Camilleri 1995; Iwanaga, 2003; Johal, 2007] These studies give the impression that success rates in patients selected by sleep endoscopy are better than average. It is not clear to what extent the situation during sleep endoscopy resembles reality. At present, however, this is the way to get closest to the real situation. A treatment plan for OSAS patients may be drawn up on the basis of a combination of the results of the polysomnography, the BMI, the examination as discussed in 1.8.1, the sleep endoscopy, and the patient’s wishes.

1.9 Conservative therapy

1.9.1 Lifestyle changes

The treatment of OSAS patients who are overweight must always begin with the advice that they have to lose weight. There is a clear link between obesity and OSAS. Peppard et al. showed the degree to which weight gain is associated with increased AHI and weight loss with decreased AHI in a normal, non-OSAS diagnosed population.[Peppard, 2000]

Additionally, obese OSAS patients who have had bariatric surgery have not only a lower BMI after the operation but also a considerably lower AHI. A survey by Haines et al. of a group of 349 patients shows a pre-operative BMI of 56 and a post-operative BMI of 38. This took the AHI down from 51 to 15.[Haines, 2007] Furthermore, the use of alcohol and sedatives must be discouraged. These substances restrain the activity of the dilatators of the upper airways.

1.9.2 Positional therapy

About half of all OSAS cases are dependent on position. That is to say that when lying on the back the AHI is more than twice as high as in the other positions. The higher the BMI, the less chance there is of position-dependent OSAS.[Oksenberg, 1997] Both Oksenberg and Maurer published surveys showing that positional therapy is indeed advantageous in position-dependent OSAS. Unfortunately, compliance is mediocre at most.[Oksenberg 2006; Maurer, 2003]

1.9.3 Nasal continuous positive airway pressure

In 1981 nasal continuous positive airway pressure (nCPAP) was introduced as a treatment of OSAS and has been considered the gold standard for treatment of severe OSAS ever since. [Sullivan, 1981] NCPAP blows air through the nose into the upper airway and works as a pneumatic splint to keep the upper airway open. NCPAP normalises the AHI and improves subjective sleepiness during the day.[Gay, 2006; Giles, 2008] It is reasonable to assume that nCPAP reduces vascular morbidity in patients with OSAS.[Buijse, 2007; Lavie, 2007] Although the scientific evidence is not conclusive.

Auto-PAP (APAP) adjusts itself to the air pressure needed, which may vary during the night and from night to night. The machine itself detects respiratory events. There is no difference in AHI, arousals, complaints or compliance between nCPAP and APAP.[Smith, 2009; Ayas, 2004] There is a subjective preference for APAP when compared to nCPAP. [Smith, 2009] Patients with congestive heart failure, significant lung disease such as chronic obstructive pulmonary disease, patients expected to have nocturnal arterial oxyhemoglobin desaturation

due to conditions other than OSAS (e.g., obesity hypoventilation syndrome), patients who do not snore (either naturally or as a result of palate surgery), and patients who have central sleep apnea syndromes are not currently candidates for APAP. Most studies evaluating APAP, regardless of the technology used, exclude such patients because the sensors and algorithms identifying respiratory events may not be sensitive or specific under these circumstances. [Morgenthaler, 2008]

Bilevel-PAP (BIPAP) makes it possible to set inspiration pressure and expiration pressure separately. The difference in pressure between inspiration and expiration supports the spontaneous inspiration by the patient who triggers his or her own inspiration as a result of the underpressure at the beginning of his inspiration. This is called pressure support. The pressure can be set lower, on average, due to the lower expiration pressure. BIPAP can bring relief to patients with pressure-related nCPAP complaints and acceptation difficulties. [Schäfer, 1998; Resta, 1999] BIPAP is also a possible form of treatment for patients with hypoventilation syndrome as BIPAP has the advantage of pressure support.[Kushida, 2006] The effectiveness and compliance of BIPAP is equal to those of nCPAP.[Gay, 2006; Kushida, 2006]

1.9.4 Mandibular Repositioning Appliance

A Mandibular Repositioning Appliance (MRA) is a brace that fixes the lower jaw forward in order to keep the upper airway open during sleep. Two meta-analyses have been carried out on the effectiveness of using an MRA.[Hoekema, 2004; Lim, 2009] Cross-over studies used in these meta-analyses have shown that the use of an MRA lowers the AHI with an average of 28.7 by an average of 14.6 points compared with a control MRA.[Mehta, 2001; Johnston, 2002; Gotsopoulos, 2002] A result of AHI<5 or a reduction of 50% exists in 63%.[Mehta, 2001; Gotsopoulos, 2002]

A MRA is an attractive treatment option for patients who do not want to be operated or use nCPAP. Besides that it is small, easy to carry and generally less expensive. Unfortunately, restrictions in the dental situation not seldom mean that a MRA cannot be fitted. These include parodontal defects, bad teeth, defects of the mandibular joint and restricted movement of the lower jaw. An MRA cannot be fitted in about one third of the cases.[Petit, 2002]. The MRA itself may also cause problems. Short-term effects include complaints of tenderness of the teeth and jaws, gum irritation, temporary bite change after removal of the appliance in the morning, excessive salivation or xerostomia. In the long term it is usually a matter of tooth movements leading to disturbed occlusion and chewing function, wear, damage to and mobility of dental elements and esthetic problems. Therefore, patients with a MRA must go for a periodic dental check-up in order to diagnose these side effects in time.

1.10 Surgical therapy

1.10.1 Nasal obstruction

From a physiological point of view it is to be expected that increasing nasal air resistance will lead to increased negative pressures and thence be conducive to collapse of the upper airway. Yet, the literature on the subject contains no indications that treatment of poor nasal passage, either conservative or surgical, leads to significant improvement of OSAS.[Kerr, 1992; Verse, 2002].

There are, however, indications that the necessary pressure for nCPAP may be reduced after operations that improve nasal passage and that, as a result, compliance may be increased. [Friedman, 2000]. In therapies where oral breathing is restricted or impossible, such as in nCPAP or MRA treatment, a good nasal passage is crucial for the success of the therapy.

Furthermore, studies have shown that patients with severe OSAS who have got tampons in their nose after an operation or an epistaxis may see their AHI rise as long as the nasal packs are in situ.[Cassisi, 1971; Wetmore, 1988; Vaartjes, 1992]. These patients must be monitored for as long as they have tampons and must, if necessary, use CPAP with a full face mask.

1.10.2 Palatal obstruction

Radiofrequency-assisted uvulopalatoplasty(Celon®)

Procedure: Energy of 1200 J is delivered with an exclusive needle device. Using this needle a triangular incision is made on both sides of the uvula and a transversal resection of the mucosa of the uvula itself. The procedure can be performed under general and local anesthesia.

Radiofrequency-assisted uvulopalatoplasty (RAUP) can be used in mild to moderate OSAS. Bassiouny published a survey of a group of 20 patients whose average AHI went down from 17.2 to 8.1.[Bassiouny, 2007]

Uvulopalatophayngoplasty/Z-palatoplasty

Procedure: When performing an UPPP a tonsillectomy is done, part of the uvula is excised and the anterior and posterior tonsillar pillars are trimmed and reoriented to create more retropalatal space.[Fujita, 1981] The first step in performing a ZPP is removing the mucosa from the palate in the shape of a butterfly. The distal margin is the free edge of the palate and the uvula; the proximal margin depends in the central line on the distance from front to back between the palate and the back wall of the pharynx and is laterally about as long as the distance between the uvula and the proximal margin of the central line. Subsequently

the uvula and the soft palate are cleft down the central line as far as the mucosa had been removed. The two flaps are swung laterally over the stripped soft palate and then stitched. [Friedman, 2004]

Uvulopalatopharyngoplasty (UPPP) has been used since 1981 to treat OSAS.[Fujita, 1981] Since then several less radical modifications of this treatment have been developed. The aim is to enlarge the retropalatal space and to decrease collapsibility. A review by Pirsig shows that the average success rate decreases from 60.5% after short-term follow-up to 47.6% after long-term follow-up.[Pirsig, 2000] In case of previous tonsillectomy Z-palatoplasty (ZPP) is indicated. Z-palatoplasty has a higher success rate than UPPP in patients without tonsils. [Friedman, 2004]

1.10.3 Retrolingual obstruction

Radiofrequent ablation of the tongue base (Celon ®)

Procedure: Energy is delivered with an exclusive needle device through the dorsal surface of the tongue. Evidence based criteria for technical adjustment and optimal energy dosage according to relevant increase in lesion size are used. According to Stuck et al. about 600 J appears to be the ideal setting for energy delivery.[Stuck, 2003] In our hospital c. 42 J is delivered at 6 lesion sides (c.252 J) in each operation session. At the time of the study, in order to reduce the risk of swelling of the tongue we did not administer 600 J at once in one session. After the initial surgical procedure, additional treatment can be given on indication. The procedure can be performed under general and local anesthesia.

Radiofrequent ablation of the tongue base (RFTB) is used to accomplish stiffening and volume reduction of the base of the tongue. There are indications that the AHI improves after RFTB in patients with mild to moderately severe OSAS. The success rate varies from 20% to 83%. These large differences can maybe explained by a variety of factors including patient selection and the amount of energy that was delivered.[Powell, 1999; Woodson, 2001; Stuck, 2002; Li, 2002; Riley, 2003; den Herder, 2006]

Hyoid suspension

Procedure: After exposure via an external horizontal incision at the level of the thyrohyoid membrane, the strap muscles (sternohyoid muscle, omohyoid muscle and thyrohyoid muscle) are divided just below the hyoid and superior to the hyoid. The tendon of the stylohyoid muscle is divided from the hyoid bone. After mobilising the hyoid bone in anterocaudal direction it is fixed permanently to the thyroid cartilage.[Riley, 1994]

Hyoid suspension (HS) is used in case of moderate to severe OSAS, with obstruction located at retrolingual level, to avoid more radical surgery such as maxillomandibular advancement or tracheostomy. This procedure, first described by Riley et al. in 1986, aims at advancement of the hyoid bone and subsequent increase of the retrolingual space.[Riley, 1986] In 1994 the intervention was modified by fixing the hyoid bone to the thyroid cartilage, instead of fixing it upward to the mandibula.[Riley, 1994] That is why this modified intervention is also frequently called hyoidthyroidpexia. Success rates of 52% and 53.3% of this revised HS have been reported.[Riley 1994; den Herder 2005]. In this thesis we will use the term HS meaning modified HS or hyoidthyroidpexia.

Genioglossus advancement

Procedure: A standard anterior mandibular osteotomy, limited to advancement of a rectangular window of the mandible including the genial tubercle and genioglossus musculature, but without rotation of the segment, is performed. The outer cortex and medulla are removed, the lingual cortical plate advanced and fixed with bone screws.[Kemer, 2002]

Like HS, Genioglossus advancement (GA) is used in case of moderate to severe OSAS, with obstruction located at retrolingual level.[Riley, 1987] There are no studies examining GA as an isolated procedure. It is only used in combination with other techniques such as uvulopalatoplasty and/or HS.

1.10.4 Maxillomandibular advancement

Procedure: A le Fort 1 osteotomy is combined with a bilateral sagittal split osteotomy of the lower jaw. Subsequently both upper and lower jaw are moved to ventral in order to enlarge the upper airway.[Prinsell, 2000]

Maxillomandibular advancement (MMA) is the most successful surgical therapy for OSAS after tracheotomy. The results are roughly comparable to the results of the use of CPAP.[Hochban, 1997] In the long term, too, the results of this operation are very successful: 90% success after an average follow-up of 51 months.[Li, 2000] The invasiveness of this treatment as well as the significant morbidity and potential side effects are reasons why this procedure should be reserved as primary surgical treatment for patients with extremely high AHI and for non-responders to multilevel surgery.

1.10.5 Tracheotomy

Procedure: A horizontal incision just below the cricoid is made through the skin, the subcutis and the platysma. The fascia between the sternothyroid muscles are vertically cleft. The thyroid

gland is moved upwards. If this is not possible, the thyroid gland is cleft and ligated. A Björk flap is made. This implies making a little flap in the trachea which remains attached caudally. Through the flap a tracheal cannula is positioned. Making a Björk flap is not necessary, but makes the introduction of the cannula and the postoperative care easier.

Tracheotomy was the first treatment performed on OSAS patients.[Kuhlo, 1969] Guilleminault [Guilleminault, 1981] and Thatcher [Thatcher, 2003] reported a success percentage of 100% in 50 and 79 patients respectively. In view of the morbidity and the impact on the patient this treatment is only performed nowadays in exceptional cases. The decision to carry out this treatment may be taken in cases of severe OSAS where conservative treatment and major surgery have failed or where there are contraindications against undergoing major surgery.

Outline of the thesis

In **Chapter 2** we evaluate whether improvements in nCPAP technology during the last years, particularly the introduction of APAP, but also more silent equipment, different masks, humidification, better education and guidance have led to better acceptance and (long-term) compliance in patients with obstructive sleep apnea syndrome (OSAS) as compared to earlier reported data in the past. In **Chapter 3** we analyse the role of sleep position in OSAS. **Chapter 4** shows the results of treating a group of patients with positional sleep apnea with position therapy. In **Chapter 5** the outcome of UPPP combined with RFTB in patients with OSAS with both palatal and retrolingual obstruction compared to the results of only UPPP is shown. In **Chapter 6** we report our surgical results of a one stage multilevel surgical approach of the upper airway (UPPP, HS, RFTB with/without GA) to treat patients with multilevel obstruction. In **Chapter 7** we investigate adverse events and complications of HS as a treatment of OSAS with obstruction only on tongue base level. In **Chapter 8** the results described in this thesis are put into a wider context. In **Chapter 9** the thesis is summarized.

chapter 2

ACCEPTANCE AND LONG-TERM COMPLIANCE OF NCPAP IN OBSTRUCTIVE SLEEP APNEA

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Abstract

In a retrospective cohort study, we evaluated whether improvements in nasal continuous positive airway pressure (nCPAP) technology, particularly the introduction of automatic adjustment of the nCPAP pressure (auto-CPAP), have led to better acceptance and (long-term) compliance in patients with obstructive sleep apnea syndrome (OSAS) as compared to earlier reported data. Questionnaires were sent to 256 patients, who were referred to our clinic for an overnight polysomnography from January 1997 to July 2005 and received nCPAP therapy for OSAS. Of the 256 patients, 24 patients were unavailable for follow-up. Of the remaining 232 patients, 58 patients (25%) had discontinued therapy, while 174 patients (75%) were still using nCPAP after 2 months to 8 years of follow-up. One hundred and thirty eight (79%) of these 174 patients used nCPAP for at least 4 h/night during ≥ 5 nights/week, 82,1% of the conventional nCPAP (fixed pressure CPAP) group (n=78) and 77,1% of the auto-CPAP group (n=96). Therefore, including the 58 failures, only 59,5% of patients can be seen as compliant. There were no statistical differences between the fixed pressure CPAP and auto-CPAP users, and between the compliant and non-compliant users according to age, BMI, AHI and Epworth Sleepiness Scale (ESS). Auto-CPAP patients used significantly more cm H_2O. The long term compliance of nCPAP therapy has have increased only slightly since the introduction of the fixed pressure CPAP 25 years ago, in spite of many efforts to improve it. It seems that a plateau has been reached and that it is unrealistic to aim at a substantially higher compliance rate.

Keywords. Obstructive sleep apnea syndrome – Nasal continuous positive airway pressure - Compliance

Introduction

Obstructive sleep apnea syndrome (OSAS) is a clinically defined syndrome associating daytime hypersomnolence and one or more of the following symptoms: severe snoring, nocturnal respiratory arrest, repeated nocturnal awakening, non-recuperative sleep and altered concentration, due to repeated obstruction of the upper airway. An apnea-hypopnea index (AHI) of more than five, obtained by overnight polysomnography, accompanied by daytime symptoms is required for the diagnosis of sleep apnea syndrome.[1] An apnea is a period of complete cessation of oronasal airflow for a minimum of 10 s; periods of more than 30% reduction in oronasal airflow, accompanied by a decrease of more than 4% in ongoing $SaO_{2,}$ are hypopneas.

The prevalence of obstructive sleep apnea in middle-aged people is 2% in women and 4% in men.[2] It has been estimated that at least 80% of all moderate and severe OSAS in the general population is likely to be missed.[3]

OSAS has adverse effects on daytime quality such as daytime sleepiness and diminished intellectual performance. OSAS is of growing significance because of its increasingly recognized high incidence and association with neurocognitive symptoms [4] and cardiovascular disease. [5] In severe OSAS, there is an increased risk to be involved in traffic accidents.[6,7] Therefore OSAS is not only treated for its symptoms, but also with the aim to reduce associated morbidity and mortality.

In 1981, nasal continuous positive airway pressure (nCPAP), which acts as a pneumatic splint, was introduced as treatment of OSAS and has been considered the gold standard for treatment of severe OSAS since.[8] It is a safe therapeutic option with few contraindications or serious side effects.[9] Unfortunately many patients experience nCPAP therapy as obtrusive and the acceptance and (long-term) compliance of nCPAP are at the most moderate. A vast body of literature was published in the last two decades on the subject of (long-term) compliance of nCPAP.[10-23] Improvements in nCPAP technology, in particular the introduction of automatic adjustments of the nCPAP pressure throughout the night (auto-CPAP),[24-29] and other attempts to enhance acceptance and compliance (positive reinforcement, psychological/ educational interventions, heated humidification) have been introduced.[30-34]

We were interested to see if these actions have led to better acceptance, adherence and long-term compliance as compared to earlier reported data. We acquired data on (long-term) compliance and therapy failure. In this paper we report the results of this follow-up obtained by questionnaires, as well as the analysis of several parameters which can predict compliance.

Methods

All patients with OSAS, as defined previously, who were offered nCPAP between January 1997 and July 2005, were included in the study. Patients with an AHI >30 were offered nCPAP as first treatment. Patients with mild to moderate OSAS (AHI <30), were also offered alternative treatments such as an oral device or surgery.

Polysomnography

From 1997 until 2001, patients were monitored with a digital CNS-sleep I/T-8 recorder (CNS Inc, Chanhassen, MN, USA) during one night at the hospital. Since 2001, polysomnography was done using a digital Embla recorder (Flaga Medical devices, Reykjavik, Iceland).

In both recorder types, polysomnography consisted of electroencephalogram (derivations: CNS-sleep I/T-8: O1-Cz; Embla: Fp2-C4/Fp1-C3), electrooculogram and submental electromyogram to record the sleep pattern. Thoracoabdominal excursions were registered by either airinflated straps (Nellcor PB; model 5702-x, in the CNS-sleep I/T-8), or by straps containing piezoelectric transducers (Embla). Pulse oximetry was used to monitor oxygen saturation (SaO_2) and heart rate. In addition ECG, movements of the limbs and the intensity of snoring were recorded. Nasal airflow was measured by a pressure sensor with the Embla recorder only.

Electrodes and sensors were placed and equipment was calibrated late in the afternoon. The system was switched on and off at 7.00 p.m. and 7.00 a.m. In case of the Embla recorder all signals were recorded with DDD (digital sampling, digital filtering, digital storage) recording technology. In both recorder types, storage was done on a PCMCIA flash-card.

The following day, the data were downloaded to the computer and analyzed by dedicated sleep software (CNS: Sleep I/T software V1.70; Embla: Somnologica 2.0.2). In both cases the data were manually reviewed by an experienced sleep investigator for final analysis.

nCPAP therapy

Following the initial positive sleep study, patients were again admitted to the hospital to titrate nCPAP therapy. During two nights in the hospital, the optimal fit of the nCPAP mask (silicone-based nose or full face masks and different intranasal systems) was determined and the optimal pressure of nCPAP therapy was established. From January 1997 until January 2002, the CPAP operating mode of the BiPAP S/T-D® (Respironics INC, Murrysville, Pennsylvania, USA) was used. The patient's optimal (fixed) level of continuous pressure (cm H_20) was found by manual titrating by an experienced EEG technician during a night session with polysomnography and video registration. Since October 2002, auto-CPAP (AutoSet® T, ResMed Limited, North Ride, Australia) was used exclusively. In between there was an overlap period in which both modalities were used.

A first notice of compliance to and problems with acceptance of nCPAP was gathered during the first two nights. Within 1 week after titration, the first evaluation took place on the pulmonary outpatient clinic. Thereafter a test period with nCPAP therapy in the home situation was started. After the test period of about 4-5 weeks, the second evaluation took place on the pulmonary department. The reports of firms responsible for nCPAP delivery were examined as were the experiences of the patients, after which a definitive form of nCPAP therapy, mask and pressure was chosen. After four months a final appointment was made.

Questionnaires

All OSAS patients, who were offered nCPAP, received questionnaires including actual nCPAP usage, a visual analogue scale for satisfaction of the therapy (a scale from zero, not satisfied, to ten, very satisfied) and questions about symptoms such as daytime sleepiness with the help of the Epworth Sleepiness Scale (ESS). We defined compliance (or adherence) as minimally 4 h/night during five nights per week of nCPAP use. Failure was defined as a refusal beforehand, withdrawal almost directly after the eligibility tests without proper evaluation or failure to reduce the AHI with nCPAP during the tests.

Statistics

All continuous variables were checked for their distributional characteristics. Whenever feasible (i.e. reasonably normally distributed), mean and standard deviation were used as statistics. Differences at baseline and after intervention between fixed pressure and auto-CPAP were tested by means of a two-sample *t* test (based on a pooled standard deviation or a Satterthwaite approximation in case of unequal variances). Categorical variables were tested by means of a Chi-square test.

Results

From January 1997 to July 2005, 256 consecutive patients were diagnosed with OSAS and offered nCPAP therapy at our hospital. Twenty-four (9.4%) patients were lost to follow-up without any information available. Data could be retrieved from 232 (90,6%) patients through returned questionnaires. The follow-up period ranged from 2 months to 8 years. Fifty-eight (25%) of these 232 patients (30 patients had fixed pressure CPAP, 28 patients had auto-CPAP) failed to actually use the therapy. Five patients died before evaluation could be obtained.

Of the evaluable 174 patients who used nCPAP, 78 patients were offered fixed pressure CPAP and 96 patients auto-CPAP. There were 65 men (83.3%) and 13 women (16,7%) in the fixed pressure CPAP group and 75 men (78,1%) and 21 women (21,9%) in the auto-CPAP group. There was no difference in any of the baseline patient characteristics between fixed pressure CPAP and auto-CPAP users (Table 1). Auto-CPAP patients used significantly more cm H_2O (P<0.0001).

Table 1 Baseline patient characteristics

	Type of CPAP		
	Fixed CPAP (N=78)	**Auto-CPAP (N=96)**	***P* value**
Age	58.2 ± 11.5	55.4 ± 11.5	0.1111
BMI	33.0 ± 7.9	33.1 ± 7.0	0.9573
AHI	47.2 ± 22.3	52.0 ± 23.1	0.1814
ESS	5.6 ± 4.5	7.1 ± 5.1	0.0530

The outcome parameters comparing the two groups are shown in Table 2. No difference in the frequency of use of nCPAP in terms of nights/week and hours/night was observed between the two groups. Also in terms of patients' satisfaction, both methods were very similar. For four patients the number of nights a week and/or the amount of time of nCPAP usage was unknown.

We defined compliance as use of nCPAP at least 4 h/night, ≥5 days/week. According to this definition, overall 138 (79%) of the 174 patients using nCPAP were compliant, 82.1% of the fixed pressure CPAP group and in 77.1% of the auto-CPAP group. Therefore, including the 58 failures, only 59,5% of patients can be seen as compliant. Except for satisfaction of nCPAP usage, no differences were observed between the patients who were compliant and the patients who were not (Table 3).

Table 2 Comparison of the use of fixed pressure CPAP and auto-CPAP in terms of nights/week and hours/night, as well according to patients' satisfaction *(excluding failures)*

Variable	**F/A**	**N**	**Mean**	**SD**	**Min.**	**Max.**	***T* test *p* value**
Nights/week	F	76	6.4	1.4	2	7	
	A	96	6.3	1.4	1	7	
	Diff (1-2)		-0.1	1.4			0.5710
Hours/night	F	75	6.5	1.5	1.5	9	
	A	95	6.3	1.8	1	11	
	Diff (1-2)		-0.1	1.7			0.6411
Satisfaction	F	76	7.5	1.9	0	10	
	A	95	7.5	2.3	0	10	
	Diff (1-2)		-0.1	2.1			0.8762

F: fixed pressure CPAP; A: auto-CPAP

Table 3 Comparison of parameters between 'compliant' and 'non-compliant' *(excluding failures)*

Variable	**C/NC**	**N**	**Mean**	**Std Dev**	**Min**	**Max**	***T* test *p* value**
Age	C	138	56.9	11.6	27	86	
	NC	33	55.3	11.7	34	79	
	Diff (1-2)		-1.6	11.6			0.4898
BMI	C	138	32.9	7.2	21.9	75.8	
	NC	32	34.2	8.4	22.3	54.6	
	Diff (1-2)		1.3	7.4			0.3777
AHI	C	131	51	21.7	9.7	123	
	NC	31	47.1	27.3	5	98	
	Diff (1-2)		-3.9	22.9			0.3974
H_2O	C	137	8.9	2.4	3	15.5	
	NC	33	8.6	2.6	4	15	
	Diff (1-2)		-0.2	2.5			0.6330
ESS	C	136	6.1	4.9	0	23	
	NC	33	7.6	4.6	0	16	
	Diff (1-2)		1.5	4.9			0.1083
Satisfaction	C	137	8	1.7	1	10	
	NC	33	5.7	2.6	0	10	
	Diff (1-2)		-2.2	1.9			<0.0001

C: compliant patients; NC: non-compliant patients; H_2O: cm H_2O pressure

Discussion

OSAS represents a relatively new disease entity, and is currently the most dynamic area in Otolaryngology/Head and Neck Surgery, both with regard to diagnostic work-up and therapy.

Treatment of OSAS is dependant on the severity of the disease and starts primarily with lifestyle changes (weight reduction, cessation of alcohol abuse, sleep hygiene), if indicated. When complains persist after these, additional therapies are needed. These can be subdivided in conservative treatment (oral device or nCPAP), surgery (minimal invasive to invasive) or combinations of both.

NCPAP has become the "gold standard" treatment of OSAS in the last decades.[35] In the pioneering phase of management of OSAS this view was understandable since uvulopalatopharyngoplasty (UPPP) was the almost exclusive surgical alternative for the treatment of OSAS and meta-analysis by Sher et al. in 1996 showed a success rate of UPPP (in unselected patients) of only 41%.[36]

To be successful, nCPAP therapy in OSAS has to be accepted by the patient. Unfortunately some patients simply refuse to use it upfront or later on, others try it but experience such serious problems such as nasal congestion and dryness, rhinorrhoea, dryness in the mouth, mask discomfort, claustrophobia, aerophagia, air leakage and irritation from device noise, that they have to give up. Other patients use nCPAP only several days a week, and/or only a limited number of hours per night sleep.

Various studies have analyzed compliance. However, the results are not always consistent, mainly because of the lack of common criteria. Furthermore, there are no precise recommendations available concerning the necessary duration of daily and weekly use. In our study 58 (25 %) of 232 patients with sufficient information available, never started nCPAP at all or stopped treatment (early). The compliance, defined as nCPAP use for minimally 4 h during five nights per week, in the remaining 174 patients in our series, was 79% (82.1% for fixed pressure CPAP vs 77.1% for auto-CPAP) as compared to earlier reported data, ranging from 46% to 89%.[10-23] Overall, only 59,5% of cases were successful, taking the non-compliant cases and the 58 (25%) failures together. Although it was to be expected that patients with a higher AHI and ESS and lower required pressure would be more compliant, no difference was found. Also age and BMI played no role of significance.

Patients with auto-CPAP used higher pressure levels than patients with fixed pressure CPAP. A reason for this statistical difference is that while titrating for fixed pressure CPAP with the auto-CPAP, the choice for the lowest pressure needed is often taken, because to minimize side effects too much pressure while not needed has to be avoided.

A limitation of our study is that the use of nCPAP in our series was estimated by the patient and not recorded by a clock-time counter, and it can therefore not be excluded that the actual use is even lower; discrepancies between subjective and objective duration and frequency of nCPAP use have been reported.[15] When looking back at 2 decades (1986 – now) [10-23] of all reported series on nCPAP use, the conclusion is that in spite of many improvements in the machinery, adjustment, intensive support, and all attempts (positive reinforcement, psychological/educational interventions, heated humidification) to increase compliance otherwise, the overall compliance has only improved marginally, if at all.

Currently we are witnessing an increasing awareness that an exciting new era in OSAS treatment is dawning. Besides the disappointing compliance rates, the use of nCPAP therapy does not change the anatomy of the upper airway and therefore patients remain dependant, lifelong. In particular for young patients, the prospect to use nCPAP lifelong is unattractive and with increasing frequency patients ask for surgical alternatives with acceptable success rates.

Also in the light of failure rates for nCPAP therapy, it is hard to maintain that nCPAP should always be preferred above other treatments. Success rates of UPPP in well selected patients (obstruction on retro palatal level only) currently reach 70-80%, as compared to the low 40% in earlier meta-analyses in non-selected patients.[37,38] In patients with obstruction at the retrolingual level comparable surgical success rates of hyoid suspension have been reported in well-selected patients.[39,40] Many other surgical and non-surgical approaches are being explored as stand-alone therapy, or in combination.[41,42] Therefore, a gradual shift can be expected to take place to alternatives to nCPAP, being a combination of surgery, lifestyle alterations and if possible positional therapy,[43,44] in well-selected, well-informed patients, while nCPAP therapy in those patients will still be in reserve in case of failure.

In conclusion, the long-term compliance of nCPAP therapy has increased only slightly since the introduction of nCPAP 25 years ago, in spite of many efforts to improve it. It seems that a plateau has been reached and that it is unrealistic to expect substantially higher compliance rates. The great challenge for the ENT-community is to accept the responsibility to endeavour to develop viable alternatives to nCPAP therapy, both for the high percentage of patients who are nCPAP failures as well as for primary treatment.

References

1. Anonymous(1999) Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 22(5):667-89
2. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep disordered breathing among middle-aged adults. N Engl J Med 328(17):1230-5
3. Young T, Evans L, Finn L, Palta M (1997) Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 20(9):705-6
4. Chesire K, Engleman H, Deary I, Shapiro C, Douglas NJ (1992) Factors impairing daytime performance in patients with sleep apnea/hypopnea syndrome. Arch Intern Med 152(3):538-41
5. Shamsuzzaman AS, Gersh BJ, Somers VK (2003) Obstructive sleep apnea, implications for cardiac and vascular disease. JAMA 290(14):1906-14
6. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J (1999) The association between sleep apnea and the risk of traffic accidents. N Engl J Med 340(11):847-51
7. George CF, Smiley A (1999) Sleep apnea and automobile crashes. Sleep 22(6):790-5
8. Sullivan CE, Issa FG, Berthon-Jones M, Eves L (1981) Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1(8225):862-5
9. Polo O, Berthon-Jones M, Douglas NJ, Sullivan CE (1994) Management of obstructive sleep apnoea/hypopnoea syndrome. Lancet 344(8923):656-60
10. Sanders MH, Gruendl CA, Rogers RM (1986) Patient compliance with nasal CPAP therapy for sleep apnea. Chest 90(3)330-3
11. Nino-Murcia G, McCann CC, Bliwise DL, Guilleminault C, Dement WC (1989) Compliance and side effects in sleep apnea patients treated with nasal continuous positive airway pressure. West J Med 150(2):165-9
12. Waldhorn RE, Herrick TW, Nguyen MC, O'Donnell AE, Sodero J, Potolicchio SJ (1990) Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest 97(1):33-8
13. Krieger J (1992) Long-term compliance with nasal continuous positive airway pressure (CPAP) in obstructive sleep apnea patients and nonapneic snorers. Sleep 15(6 Suppl):S42-6
14. Hoffstein V, Viner S, Mateika S, Conway J. (1992) Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis 145(4 Pt 1):841-5
15. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF (1993) Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 147(4):887-95
16. Rauscher H, Formanek D, Popp W, Zwick H (1993) Self-reported vs measured compliance with nasal CPAP for obstructive sleep apnea. Chest 103(6):1675-80
17. Meurice JC, Dore P, Paquereau J, Neau JP, Ingrand P, Chavagnat JJ, Patte F (1994) Predictive factors of long-term compliance with nasal continuous positive airway pressure treatment in sleep apnea syndrome. Chest 105(2):429-33

18. Pieters T, Collard P, Aubert G, Dury M, Delguste P, Rodenstein DO (1996) Acceptance and long-term compliance with nCPAP in patients with obstructive sleep apnoea syndrome. Eur Respir J 9(5):939-44
19. Lojander J, Maasilta P, Partinen M, Brandler PE, Salmi T, Lehtonen H (1996) Nasal-CPAP, surgery, and conservative management for treatment of obstructive sleep apnea syndrome. A randomized study. Chest 110(1):114-9
20. Pepin JL, Krieger J, Rodenstein D, Cornette A, Sforza E, Delguste P, Deschaux C, Grillier V, Levy P (1999) Effective compliance during the first 3 months of continuous positive airway pressure. A European prospective study of 121 patients. Am J Respir Crit Care Med 160(4):1124-9
21. Popescu G, Latham M, Allgar V, Elliott MW (2001) Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. Thorax 56(9):727-33
22. Hui DS, Choy DK, Li TS, Ko FW, Wong KK, Chan JK, Lai CK (2001) Determinants of continuous positive airway pressure compliance in a group of Chinese patients with obstructive sleep apnea. Chest 120(1):170-6
23. Sin DD, Mayers I, Man GC, Pawluk L (2002) Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study. Chest 121(2):430-5
24. Fung C, Hudgel DW (2000) A long-term randomized, cross-over comparison of auto-titrating and standard nasal continuous airway pressure. Sleep 23(5):645-8
25. Teschler H, Wessendorf TE, Farhat AA, Konietzko N, Berthon-Jones M (2000) Two months auto-adjusting versus conventional nCPAP for obstructive sleep apnoea syndrome. Eur Resp J 15(6):990-5
26. d'Ortho MP, Grillier-Lanoir V, Levy P, Goldenberg F, Corriger E, Harf A, Lofaso F (2000) Constant vs. automatic continuous positive airway pressure therapy: home evaluation. Chest 118(4):1010-7
27. Randerath WJ, Schraeder O, Galetke W, Feldmeyer F, Ruhle KH (2001) Autoadjusting CPAP therapy based on impedance efficacy, compliance and acceptance. Am J Respir Crit Care Med 163(3 Pt 1):652-7
28. Hukins C (2004) Comparative study of autotitrating and fixed-pressure CPAP in the home: a randomized, single-blind crossover trial. Sleep 27(8):1512-7
29. Hussain SF, Love L, Burt H, Fleetham JA (2004) A randomized trial of auto-titrating CPAP and fixed CPAP in the treatment of obstructive sleep apnea-hypopnea. Respir Med 98(4)330-3
30. Massie CA, Hart RW, Peralez K, Richards GN (1999) Effects of humidification on nasal symptoms and compliance in sleep apnea patients using positive airway pressure. Chest 116(2):403-8
31. Hoy CJ, Vennelle M, Kingshott RN, Engleman HM, Douglas NJ (1999) Can intensive support improve continuous positive airway pressure use in patients with sleep apnea/hypopnea syndrome? Am J Respir Crit Care Med 159(4 Pt 1):1096-100
32. Duong M, Jayaram L, Camfferman D, Catcheside P, Mykytyn I, McEvoy RD (2005) Use of heated humidification during nasal CPAP titration in obstructive sleep apnoea syndrome. Eur Respir J 26(4):679-85
33. Jean Wiese H, Boethel C, Phillips B, Wilson JF, Peters J, Viggiano T (2005) CPAP compliance: video education may help! Sleep Med 6(2):171-4

34. Mador MJ, Krauza M, Pervez A, Pierce D, Braun M (2005) Effect of heated humidification on compliance and quality of life in patients with sleep apnea using nasal continuous positive airway pressure. Chest 128(4):2151-8

35. (1994) Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Official statement adopted March 1944. Am J Respir Crit Care Med 150:1738-45

36. Sher AE, Schechtman KB, Piccirillo JF (1996) The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 19(2):156-77

37. Friedman M, Ibrahim H, Joseph NJ (2004) Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope 114(3):454-9

38. 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(2):19-25

39. den Herder C, van Tinteren H, de Vries N (2005) Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. Laryngoscope 115(4):740-5

40. Goldberg AN, Kezirian EJ (2006) Hypopharyngeal surgery in obstructive sleep apnea: an evidence-based medicine review. Arch Otolaryngol Head Neck Surg 132(2):206-13

41. Verse T, Baisch A, Maurer JT, Stuck BA, Hörmann K (2006) Multilevel surgery for obstructive sleep apnea: Short-term results. Otolaryngol Head Neck Surg 134(4):571-7

42. Richard W, Kox D, den Herder C, van Tinteren H, de Vries N (2007) One stage multilevel surgery (uvulopalatopharyngoplasty, Hyoid Suspension, Radiofrequent Ablation of the Tongue Base with/without Genioglossus Advancement) in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 264(4):439-44

43. Oksenberg A, Silverberg DS, Arons E, Radwan H (1997) Positional versus non-positional obstructive sleep apnea patients. Chest 112(3):629-39

44. Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N (2006) The role of sleep position in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 263(10):946-50

chapter 3

THE ROLE OF SLEEP POSITION IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Abstract

We analyzed the role of sleep position in obstructive sleep apnea syndrome (OSAS). The polysomnograms of 120 patients with sleep apnea syndrome were analyzed. We associated the apnea hypopnea index (AHI) of the supine position with the AHI of the other positions. Patients were stratified in a group of positional patients (PP) (AHI supine ≥ 2 x AHI other positions) and a group of non-positional patients (NPP). In 55.8% of our patients, OSAS was position dependent. PP patients were significantly (6.7 years) younger. BMI and AHI were higher in the NPP group, but the difference was not significant. Level of obstruction in the upper airway (retropalatinal versus retrolingual versus both levels) as assessed by sleep endoscopy was not significantly different between the two groups. Total sleep time (TST) was equal in both groups, but the average time in supine position was 37 min longer in the PP group. This study confirms the finding that in more than 50% of patients, OSAS is position dependent. Apart from age, no patient characteristics were found indicating the position dependency. Overall AHI does not identify positional OSAS.

Key words. Body position – Obstructive sleep apnea syndrome

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common clinical problem.[1] The prevalence of OSAS in middle-aged people (30-60 years) is 2% in women and 4% in men.[2] In practice obstructive sleep apnea seems to be under-reported; roughly 85% of patients with obstructive sleep apnea are undiagnosed.[3] Due to longer life-expectancy and increase in weight in the general population, its incidence can be expected to rise.

OSAS is characterized by periods of cessation and reduction of the oronasal airflow during sleep accompanied by desaturations of blood oxygen. This sleep related breathing disorder is a result of abnormal anatomy (crowding of the upper airway) superimposed on normal sleep physiology (reduction of muscle tone).

Clinical symptoms are (in descending order of frequency) snoring, unquiet sleep, daytime fatigue, diminished intellectual ability and changes in personality. If OSAS remains untreated, patients are at higher risk to develop cardiovascular diseases.[4-9] In case of AHI > 40 the risk to be involved in a traffic accident increases.[10]

Treatment of OSAS consists of lifestyle alterations such as weight reduction and reducing alcohol, sedatives and sleep medication. Conservative interventions include mandibular repositioning advancements in mild to moderate OSAS, and nasal continuous positive airway pressure (NCPAP) in severe OSAS.[11,12] NCPAP acts as a pneumatic splint, which dilates the airway and prevents its collapse during sleep. However, up to 50% of patients are not willing to start or to comply to NCPAP therapy.[13,14] Also, a variety of surgical modalities is frequently applied.

Although many patients snore louder and have more apneas in supine position only a limited number of studies have been reported on the role of sleep position [15-21] and, subsequently, interventions to decrease the severity of OSAS by influencing sleep position.[22] In this paper we present our analysis of the role of sleep position in OSAS.

Methods

We analyzed the overnight polysomnograms of all patients who visited our department from March 2003 to January 2005 because of habitual snoring and/or suspicion of OSAS. Polysomnography was recorded using a digital polygraph system (Embla, Flaga Medical

Devices, Reykjavik, Iceland). Electroencephalogram (Fp2-C4/Fp1-C3), electrooculogram and submental electromyogram were used to record the sleep pattern. Nasal airflow was measured by a pressure sensor. Thoracoabdominal excursions were registrated by straps containing piezoelectric transducers. Pulse oximetry was used to monitor oxygen saturation (SaO2) and heart rate. In addition ECG, movements of the limbs and the intensity of snoring were recorded.

Body position was determined by a position sensor (Pro-Tech, Woodinville, WA, USA), which was attached to the midline of the abdominal wall. This sensor differentiated between the upright, left side, right side, prone and supine position. All signals were recorded with 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. We considered unknown position as non-supine, because the sensor only gives unclear registration (fluttering) when patients turn to other positions or when patients sleep in intermediate position (half on the back and half on the side).

Patients who met the criteria for OSAS and in whom surgical therapy was considered, underwent sleep endoscopy under midazolam or propofol sedation to investigate the level of obstruction of the upper airway and soft tissue collapse.[23,24]

The recommended diagnostic criteria for OSAS include an apnea hypopnea index (AHI) of five or more and evidence of daytime sleepiness.[25] The AHI is the mean number of apneas and hypopneas per hour during sleep. An apnea is a period of 10 s without oronasal airflow. A hypopnea is an episode of more than 30% airflow reduction of the baseline (calculated from the preceding period of 100 s) during at least 10 s. Suggested AHI thresholds are 5, 15 and 30 events per hour for mild, moderate and severe levels of OSAS, respectively.[25] We defined position dependent OSAS as an at least two times higher AHI in supine position than the average AHI in the other positions. To score the severity of daytime sleepiness, we used the Epworth Sleepiness Scale (ESS).[26] Patients who had an AHI between five and ten had to have at least an ESS score of seven to be included in this study.

Statistical methods

All measurements of all patients were used. Differences between the PP and the NPP group were calculated by means of the Wilcoxon two-sample test for continuous variables and with the Fisher's exact test or the Cochran-Armitage trend test for ordered categories. To calculate the difference between the AHI in REM sleep and the AHI in NREM sleep we used the Signed Rank test.

Results

A total of 120 patients, 102 men and 18 women, with a mean age of 50.1 years, met the criteria of OSAS, diagnosed by polysomnography and Epworth Sleepiness Scale, and underwent sleep endoscopy under midazolam or propofol sedation. The mean AHI and BMI were 22.8 and 28.2, respectively.

Table 1 Position dependency in relation to age, BMI, AHIav, AHI supine and AHIav in other positions

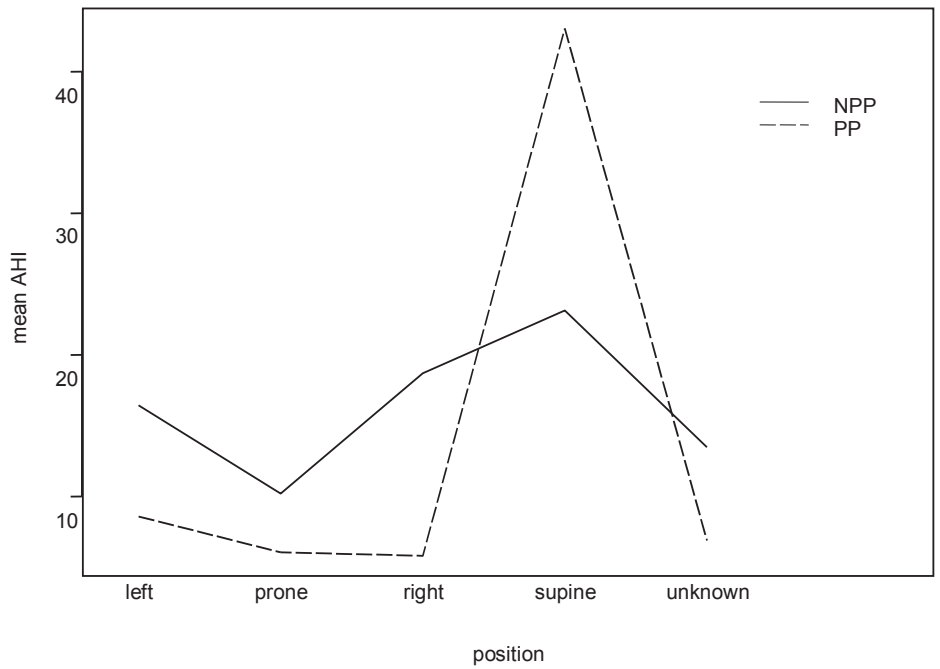
Variable	NPP/PP	N	Mean	SD	Wilcoxon *P*-value
Age	NPP	53	53.9	11.0	
	PP	67	47.1	11.5	
	Diff (1-2)		6.7	11.3	0.0040
BMI	NPP	53	28.6	4.8	
	PP	67	27.9	3.4	
	Diff (1-2)		0.7	4.1	0.5709
AHIav	NPP	53	24.7	16.3	
	PP	67	19.1	9.6	
	Diff (1-2)		5.7	12.9	0.1018
AHI supine	NPP	53	23.1	23.2	
	PP	67	43.0	19.4	
	Diff (1-2)		-19.9	21.1	<0.0001
AHI other positions	NPP	53	23.9	15.3	
	PP	67	8.2	7.9	
	Diff (1-2)		15.8	11.8	<0.0001

PP: position-dependent patients; NPP: non-position dependent patients; Diff: difference; AHIav: average AHI

Of the 120 subjects, 67 (55.8%) patients were position dependent (PP) and 53 (44.2%) were non-positional patients (NPP). In the position dependent group, a total of 60 patients (89,6%) had an AHI< 20 in the non-supine position. Table 1 shows how position dependency is related to age, BMI and AHI. The PP group was significantly younger; the difference in mean age between the two groups was 6.7 years. Although BMI and AHI were slightly higher in the non-positional group, these differences were not significant. However, there were significant differences between the AHI in supine position and the mean AHI of the other positions between the NPP and the PP group. The PP group has a significantly higher AHI in the supine position than the NPP group, while the NPP group has a higher average AHI in the other positions. Figure 1 shows the mean AHI of all different positions for the NPP and PP group. In

Fig. 2 the extent of the differences between the AHI in supine position and the average AHI of the other positions divided in the PP and NPP group are shown.

Figure 1 Mean AHI of NPP and PP for different positions



A comparison of sleep parameters is shown in Table 2. There is no difference in total sleep time (TST) between the groups. However, the TST in supine position differed significantly. The average time in supine position was 37 min longer in the PP group. The percentage of REM sleep is equal for the groups. The REM index (AHI in REM sleep) is significantly higher in the NPP group and although there is no significance, the mean oxygen saturation in this group is lower.

The mean REM index is 25.7 and the mean NREM index 21.2. The overall REM index is significantly higher than the NREM index (*P*=0.0204).

Figure 2 Difference between AHI in supine position and mean AHI of the other positions.

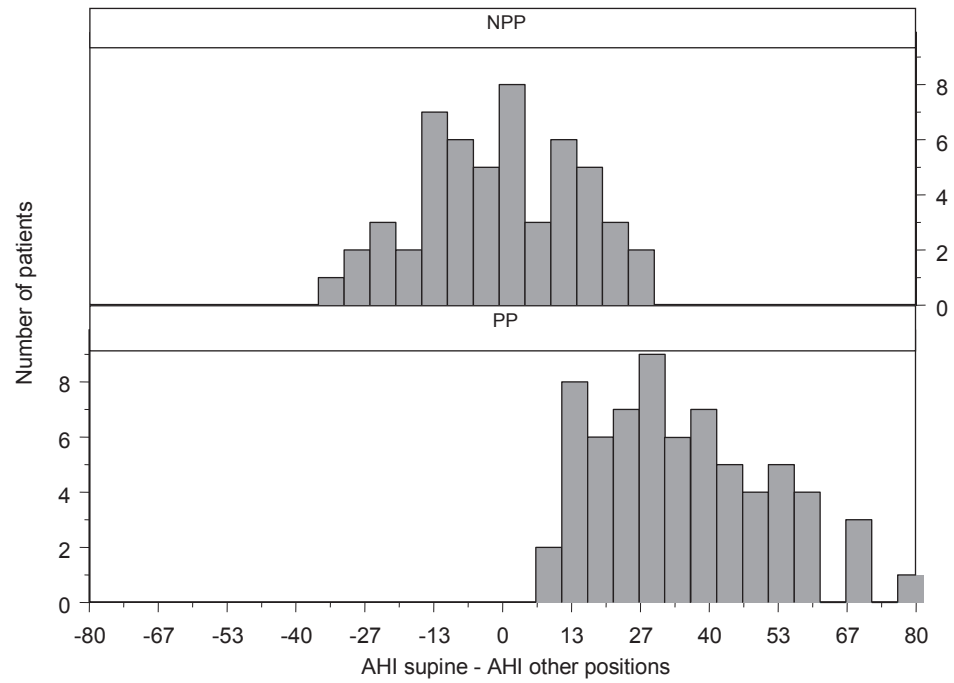


Table 2 Comparison of sleep parameters between the NPP and PP group

Variable	NPP (*N*=53)	*PP (N=67)*	Wilcoxon *P*-value
TST total	367.5	404.5	0.2276
TST supine	98.9	136.1	0.0132
TST other positions	268.6	268.3	0.9979
% REM	20.5	21.0	0.8043
REM index	30.8	21.7	0.0181
NREM index	22.6	20.1	0.7180
Mean SaO2 REM	94.3	95.1	0.0551

TST: total sleep time (min); REM index: AHI in REM sleep; NREM index: AHI in NREM sleep; SaO2: oxygen saturation

The level of obstruction did not differ significantly, although there were more patients with obstruction at tongue base level in the PP group (Table 3).

Table 3 Level of obstruction

	Level of obstruction			
Frequency Row Pct	**Multilevel**	**Palatinal**	**Tongue Base**	**Total**
NPP	28	21	4	53
	52.8	39.6	7.6	100
PP	30	24	13	67
	44.8	35.8	19.4	100
Total	58	45	17	120

Multilevel: palatinal and tongue base

Discussion

In the present study 55.8% of the 120 patients had position dependant OSAS. Arbitrarily, we defined position dependent OSAS as an at least two times higher AHI in supine position than the mean AHI in the other positions. Oksenberg et al. [18] found a remarkably similar percentage (55.9% positional OSAS) in a series of 574 patients. BMI and AHI were higher in our non-positional group, although not significantly. In their series the BMI and the AHI were significantly higher in the NPP group. Similar to their series, our patients with positional OSAS were significantly (6.7 years) younger than non-positional patients.

We found that in mild to moderate OSAS, position dependency is common; in severe OSAS non-position dependency occurs relatively more frequently. It is tempting to postulate that in the continuum of mild to moderate to severe OSAS, the etiologic role of body position during sleep gradually changes. Apparently, with increasing AHI, turning to the lateral position is not efficient anymore. Cartwright et al.[17] showed that patients with positional sleep apnea prefer the lateral position over the supine position in REM sleep. It is remarkable that in our study PP patients sleep significantly longer (37 min) in supine position. We found that overall, the AHI in REM sleep is significant higher than in non-REM sleep. A lower percentage of REM sleep in the PP group is a possible reason that PP sleep longer on their back, but in this study we found no difference in the percentage REM sleep between the groups. What we did see is that the oxygen saturation in REM sleep, although not significant, is lower in the NPP group.

Body position shifts from the supine to the lateral position is more effective for non-obese than for obese patients.[16,18,20,21] Nevertheless, even NPP benefit of sleeping in the lateral position since the severity of the apneic events occurring while sleeping in the lateral position is less than in the supine position.[19]

Ours is the first study in which the level of obstruction in the upper airway (retropalatal vs retrolingual or both) is associated with body posture during sleep. We routinely perform sleep endoscopy with midazolam or propofol in patients with OSAS in whom surgery is considered.[23,24] We hypothesized that in patients with retrolingual obstruction, more position dependency would occur, but this was not the case. Although there were indeed more patients with obstruction at tongue base level in the PP group (Table 3), the level of obstruction (retropalatinal vs retrolingual vs multilevel) did not differ significantly.

Positional therapy can be defined as preventing patients to sleep in supine position. Patients are often advised to stitch a tennis ball in the back of their pyamas, but the adherence to this kind of intervention is poor, probably because it is uncomfortable, and in practice this kind of advice is rarely followed. In the present observational study, the effectiveness of such intervention was not investigated. It is surprising that given the considerable influence of sleep position on the severity of OSA, so little effort is put in developing effective and comfortable-to-wear devices that influence sleeping posture. We found that 89,6% of the positional patients had a mean AHI <20 in non-supine position. Some devices as special pillows are on the market, but the effect of these have not been tested. Recently, Maurer et al. [22] tested the efficacy of a vest preventing the supine position in a group of only 12 patients. Nine patients (75%) were cured (AHI <10, AHI reduction >50%), two (17%) patients improved (AHI reduction >50%) and one patient remained unchanged. The TST at an oxygen saturation below 90% was reduced from 11.7 to 1.5.

In conclusion, our data confirm the important role of body posture during sleep on the occurrence and severity of sleep apnea. In a selected group of patients, prevention of sleeping in supine position could seriously decrease the AHI. In positional OSAS, the potential role of positional therapy is insufficiently investigated. It is postulated that positional therapy could be of value both as single treatment in simple snoring and mild OSAS, and could be used as additional treatment to standard therapies in more severe cases as well.

References

1. Flemons WW (2002) Clinical practice. Obstructive sleep apnea. N Engl J Med 347(7):498-504
2. Young T, Palta M, Dempsey J, Skatrud J, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328(17):1230-5
3. Young T, Evans L, Finn L, Palta M (1997) Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 20(9):705-6
4. Shamsuzzaman ASM, Gersh BJ, Somers VK (2003) Obstructive sleep apnea, implications for cardiac and vascular disease. JAMA 290(14):1906-14
5. Phillipson EA. Sleep apnea-a major public health problem (1993) N Engl J Med 328:1271-3
6. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM (2001) Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health study. Am J Respir Crit Care Med 163:19-25
7. Marin JM, Carrizo SJ, Vicente E, Agusti AG (2005) Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 365(9464):1046-53
8. Dyken ME, Somers VK, Yamada T, Ren ZY, Zimmerman MB (1996) Investigating the relationship between stroke and obstructive sleep apnea. Stroke 27:401-7
9. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342:1378-84
10. George CF, Smiley A (1999) Sleep apnea and automobile crashes. Sleep 22:790-5
11. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18(6):501-10
12. Jenkinson C, Davies RJ, Mullins R, Stradling JR (1999) Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet 353(9170):2100-5
13. Grunstein RR (1995) Nasal continuous positive airway pressure treatment for obstructive sleep apnoea. Thorax 50:1106-13
14. Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes: Statement of the American Thoracic Society. (1994) Am J Crit Care Med 150:1738-45
15. Cartwright RD (1984) Effect of sleep position on sleep apnea severity. Sleep 7:110-4
16. George CF, Millar TW, Kryger MH (1988) Sleep apnea and body position during sleep. Sleep 11(1)90-9
17. Cartwright RD, Diaz F, Lloyd S (1991) The effect of sleep posture and sleep stage on apnea frequency. Sleep 14(4):351-3
18. Oksenberg A, Silverberg DS, Arons E, Radwan H (1997) Positional vs nonpositional obstructive sleep apnea patients. Chest 112:629-39

19. Oksenberg A, Khamaysi I, Silverberg DS, Tarasiuk A (2000) Association of body position with severity of apneic events in patients with severe nonpositional obstructive sleep apnea. Chest 118:1018-24
20. Itasaka Y, Miyazaki S, Ishikawa K, Togawa K (2000) The influence of sleep position and obesity on sleep apnea. Psychiatry Clin Neurosci 54(3):340-1
21. Akita Y, Kawakatsu K, Hattori C, Hattori H, Suzuki K, Nishimura T (2003) Posture of patients with sleep apnea during sleep. Acta Otolaryngol 550:41-5
22. Maurer JT, Stuck BA, Hein G, Verse T, Hörmann K (2003) Schlafapnoetherapie mit einer neuartigen rückenlage-verhinderungs-weste. Dtsch Med Wochenschr 128:71-5
23. Hessel NS, de Vries N (2002) Diagnostic work-up of socially unacceptable snoring. II Sleependoscopy. Eur Arch Otorhinolaryngol 259:158-61
24. Den Herder C, van Tinteren H, de Vries N (2005) Sleep endoscopy versus modified Mallampati score in sleep apnea and snoring. Laryngoscope 115(4):735-9
25. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. (1999) The report of an American academy of sleep medicine task force. Sleep 22(5):667-89
26. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14(6):540-5

chapter 4

EVALUATION OF A NEW SIMPLE TREATMENT FOR POSITIONAL SLEEP APNEA PATIENTS

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Abstract

Obstructive sleep apnea syndrome is a common clinical problem. Positional sleep apnea syndrome, defined as having a supine apnea hypopnea index twice or more as compared to the apnea hypopnea index in the other positions, occurs in 56% of obstructive sleep apnea patients. A limited number of studies focuses on decreasing the severity of sleep apnea by influencing sleep position. In these studies an object was strapped to the back (tennis balls, squash balls, special vests), preventing patients from sleeping in the supine position. Frequently, this was not successful due to arousals whilst turning from one lateral position to the other, thereby disturbing sleep architecture and sleep quality. We developed a new, neck worn, device which influences sleep position by offering a vibration when in supine position, without significantly reducing total sleep time. Thirty patients with positional sleep apnea were included in this study. No side effects were reported. The mean apnea hypopnea index dropped from 27.7±2.4 to 12.8±2.2. Seven patients developed an overall apnea hypopnea index below 5 when using the device in ON modus. We expect that positional therapy with such a device can be applied as single treatment in many patients with mild to moderate position dependent obstructive sleep apnea, while in patients with a more severe obstructive sleep apnea such a device could be used in combination with other treatment modalities.

Key words. positional treatment - obstructive sleep apnea

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common clinical problem.[1] The prevalence of OSAS in middle aged people (30-60 years) is 2% in women and 4% in men.[2] The prevalence of sleep apnea seems to be under-reported; roughly 85% of patients remain undiagnosed.[3] Due to longer life-expectancy and increase in weight in the general population, its incidence can be expected to rise.

OSAS is characterized by periods of cessation and reduction of the oronasal airflow during sleep accompanied by desaturations of blood oxygen. This sleep related breathing disorder is a result of abnormal anatomy (crowding of the upper airway) superimposed on physiologic or excessive reduction of muscle tone during sleep.

Clinical symptoms are (in descending order of frequency) snoring, restless sleep, daytime fatigue, diminished intellectual ability and changes in personality. If OSAS remains untreated, patients are at higher risk of developing cardiovascular diseases.[4-9] Furthermore, in case of an AHI > 40 the risk of being involved in a traffic accident increases.[10]

Conservative treatment of OSAS consists of lifestyle alterations such as weight reduction and reducing intake of alcohol and sedatives. Interventions include mandibular repositioning appliances and surgery in mild to moderate OSAS and continuous positive airway pressure (CPAP) in moderate to severe OSAS.[11,12] All these treatment modalities are costly and have downsides. Many patients refuse or simply cannot tolerate CPAP. Others only use CPAP a few hours per night, every night or only some nights.[13,14] Treatment with oral devices is reasonably effective for snoring and mild to moderate sleep apnea, but has side effects such as jaw discomfort, hypersalivation or a dry mouth, while in the long term dental occlusion might change. In addition, up to 1/3 of patients have contraindications for oral device therapy.[15] Last but not least, mediocre results, pain, and complications are associated with OSAS surgery.

A limited number of studies have been published on the role of sleep position in OSAS.[16-23] In two studies from Israel and the Netherlands a remarkable steady 56% of patients have positional sleep apnea, defined as a supine AHI twice or more as compared to the AHI in the other positions.[19,20,23] An additional 30% of patients have a higher AHI in supine position than in the other positions, but not twice as high. Attempts to decrease the severity of sleep apnea by influencing sleep position have been reported but with limited success.[24-27] The discomfort and disruption of sleep architecture have been responsible for poor compliance and subsequent disappointing results of these interventions. In this paper we present our

experience with a new, neckworn, device which influences the role of sleep position in sleep apnea, while getting around the problem of disrupted sleep quality.

Methods

Study design

Consecutive patients, aged >18years, who were referred to the Department of Otorhino-laryngology, Head and Neck Surgery of the Saint Lucas Andreas Hospital (Amsterdam, The Netherlands) and who were diagnosed, using full overnight in-hospital polysomnography, with positional sleep apnea (AHI > 5, AHI supine ≥ 2 x AHI other positions, percentage of total sleep time in supine position ≥ 10% and ≤ 90%) were requested to participate in this study. In addition to the first baseline polysomnography, patients underwent two more in-hospial test polysomnographies after they had given written informed consent. These two test recordings were scheduled with at least one week in between, so that possible sleep deprivation resulting from the first recording would not influence the second. During the test recordings patients wore the electronic device attached to their neck. Randomly, in one of the two test recordings the device was active, in the other it was inactive. Patients were blinded for the chosen activity state of the device. The study was approved by the local human research ethics review board.

Polysomnography

Polysomnogram recordings were carried out using a digital polygraph system (Embla A10, Broomfield, USA). This records the electroencephalogram (FP2-C4/C4-O2), electrooculogram, EKG and submental and anterior tibial electromyogram. Nasal airflow was measured by a pressure sensor and arterial oxygen saturation by finger pulse oximetry. Thoraco-abdominal motion was recorded by straps containing piezoelectric transducers. Snoring was recorded through a piezo snoring sensor. Body position was determined by a position sensor (Sleepsense, St. Charles, USA), which was attached to the midline of the upper abdominal wall. This sensor differentiated between the upright, left side, right side, prone and supine position. All signals were recorded with DDD (digital sampling, digital filtering, digital storage) recording technology and a sample rate up to 200 Hz. Storage was done on a PCMCIA flash-card. The following day, data were downloaded to the computer and analyzed by dedicated sleep software (Somnologica, Broomfield, USA). The data were manually reviewed for analysis by an experienced sleep investigator, blinded for the activity state of the device.

Device

The device consisted of a small vibrating apparatus (3x3x1 cm, powered by small batteries, see figure 1A) similar to the silent alarm device used in mobile phones. This silent, vibrating alarm

was triggered by a position sensor. The position sensor started the trigger with a delay of 10 seconds after the supine position was detected, causing the device to vibrate with gradually incremental strength for as long as it took the position sensor to detect another position, in which case the vibrations ceased immediately. The small device was worn secured to the skin of the neck with hypo-allergenic adhesive tape (figure 1B) and connected to the polysomnograph system.

Figure 1A Device (scale in cm)

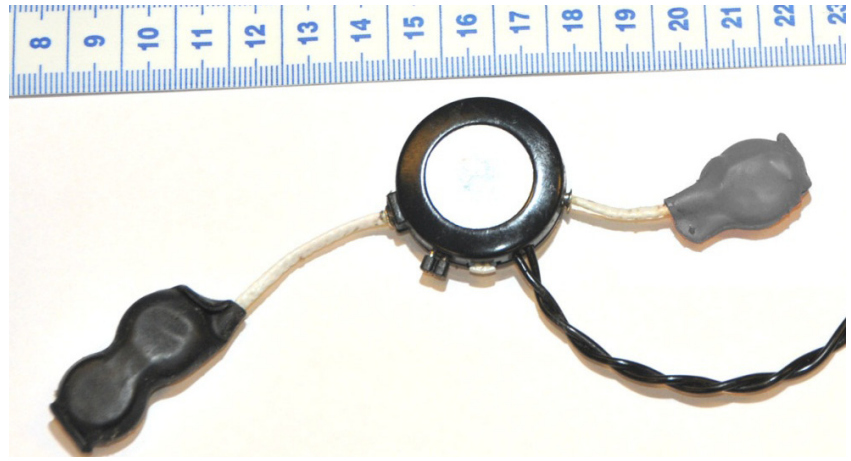
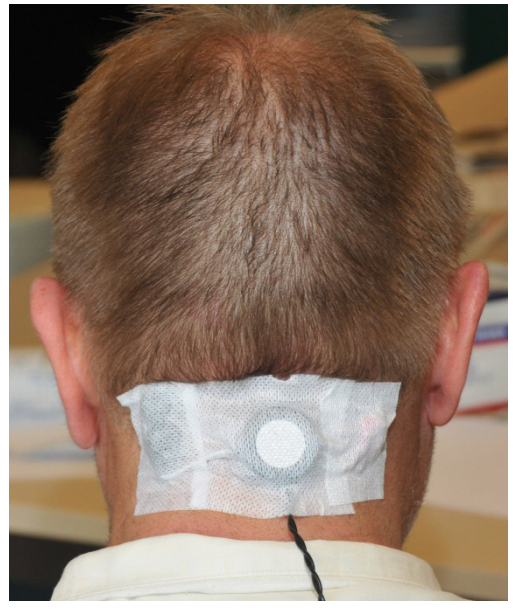
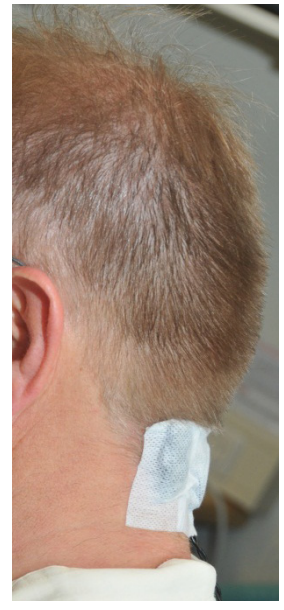


Figure 1B Device attached with hypo-allergenic adhesive tape





1A,B: The middle part (ring structure) of the apparatus shown consists of a small vibrating motor (like the one used in cell phones) and a position sensor. Three small round batteries (2 positioned on the left, 1 on the right) are connected via the white cables. The braided black cables connect the device to the polysomnograph system.

Definitions

The recommended diagnostic criteria for obstructive sleep apnea syndrome include an apnea hypopnea index (AHI) of 5 or more and evidence of daytime sleepiness. The AHI is the mean number of apneas and hypopneas per hour during sleep. An apnea is a period of 10 seconds without oronasal airflow. A hypopnea is an episode of more than 30% airflow reduction of the baseline (calculated from the preceding period of 100 seconds) during at least 10 seconds. Suggested AHI thresholds are 5, 15 and 30 events per hour for mild, moderate and severe levels of OSAS, respectively.[28] Desaturation index was defined as the number of desaturations ≥ 4% for a minimum of 10 seconds per hour of sleep. We defined position dependent OSAS as an at least two times higher AHI in supine position than the average AHI in the other positions.[19] For the analysis of overall sleep quality during the night we used the sleep efficiency (defined as duration of sleep as percentage of time spent in bed) and deep sleep quantity (as percentage of total sleep time). Arousals were defined as abrupt shifts from sleep (of at least 10 seconds duration) to faster EEG activities. Awakenings were defined as return to the polysomnographically defined awake state from any NREM or REM sleep stages.

Data analysis

Data were analyzed using Excel 2003 (Microsoft, Redmond, WA) and the SPSS statistical package (version 16, SPSS Inc, Chicago, IL). Differences between test situations were calculated by means of paired Student's t-Tests. Some of the parameters are not strictly normally distributed. Despite the latter, Student's T-test is robust enough to take on slight deviations of normality. If necessary results were verified using non-parametric Wilcoxon signed ranks test. P values > 0.05 were considered as non-significant. Beforehand the decision was made to analyse the results on an intention to treat basis. Thus patients who would not tolerate wearing the device or in whom the device would malfunction were not excluded from analysis.

Results

30 Patients were included in this study during a period of 18 months. In these patients the third PSG was performed one to 3 months, median 1.5 months, after the first PSG (Table 1). Individual body mass indices over time did not differ more than 0.2 kg/m^2.

Table 1 Baseline characteristics of all patients

Measurement	Total subjects *(N=30)*
Age (years)	48.0 ± 9.5
Body mass index (kg/m^2)	27.7 ± 3.6
Male : female ratio	6 : 1
Median months from PSG 1 to 3	1.5

Age and body mass index are shown as mean ± standard deviation.

Polysomnography results were divided in three groups. No device (ND), device attached in OFF modus (DOFF) and device attached in ON modus (DON). Display of p-values will be as follows: between ND and DOFF, between ND and DON and between DOFF and DON.

Analysis of polysomnography data showed that the device worked well in 27 patients. All patients slept at least some time of each (ND, DOFF, DON) of the 3 nights in a supine position. In 3 patients the device did not work properly. According to the position sensor in these patients, despite an episode of supine position, the device did not vibrate. The analysis was performed on intention to treat basis and these patients were not excluded from analysis.No side effects were reported.

The effect of the device on the mean sleep parameters is shown in Table 2. Highlighted values indicate significance.

In figure 2A, B and C the effect of the device on apnea hypopnea index, supine AHI and non supine AHI for each individual patient are shown. The thicker line shows the mean value for all patients. Although wearing the device in OFF modus already had a significant effect on the AHI, the decrease in AHI was much larger when the device was worn in ON modus. Differences in AHI between ND and DOFF and between DOFF and DON did not seem to have been affected by sleeping the first or the second night with the device attached in ON modus (Figure 3A and B).

The average percentage of total sleep time spent in supine position significantly decreased from 40.0 (ND) and 40.0% (DOFF) to 19.0% (DON) when the device was worn in ON modus (p=0.93, 0.00, 0.00) (Figure 4). Individuals who wore the device in ON modus the first night did not seem to avoid the supine position more effectively the second night (without vibration) compared to those who wore the device off in the first night (data not shown). This could be due to the time (one to two weeks) in between the two recordings.

Table 2 Effect of device on mean sleep parameters

	ND	DOFF	DON	*p ND DOFF*	*p ND DON*	*p DOFF DON*
AHI (/h)	27.7±2.4	23.5±2.6	12.8±2.2	*0.04*	*0.00*	*0.00*
Supine AHI (/h)	59.7±3.6	45.0±4.8	12.5±3.1	*0.00*	*0.00*	*0.00*
% of TST in supine position	40.0±3.5	40.0±4.5	19.0±4.1	*0.93*	*0.00*	*0.00*
Non supine AHI (/h)	6.7±1.2	13.4±2.7	11.2±2.2	*0.02*	*0.03*	*0.49*
% TST non supine position	58.5±3.6	55.5±4.9	78.5±4.0	*0.63*	*0.00*	*0.00*
AHI REM (/h)	21.1±4.2	24.6±4.9	16.2±4.3	*0.25*	*0.35*	*0.29*
% REM	21.7±1.2	18.3±1.5	19.2±1.5	*0.11*	*0.27*	*0.67*
AI (/h)	16.3±2.3	11.5±1.6	3.4±0.8	*0.01*	*0.00*	*0.00*
desaturation index (/h)	11.5±1.7	9.7±1.8	4.6±1.1	*0.26*	*0.00*	*0.01*
mean oxygen saturation (%)	95.2±0.3	95.2±0.3	95.6±0.2	*0.24*	*0.20*	*0.34*
sleep efficiency (%)	91.9±1.4	89.9±1.6	88.3±1.8	*0.21*	*0.10*	*0.59*
TST (min)	436±11.4	417±10.6	393±9.7	*0.14*	*0.00*	*0.13*
arousal index (/h)	9.0±1.1	9.9±1.0	6.8±0.7	*0.77*	*0.04*	*0.01*
number of awakenings	3.4±0.6	3.9±0.9	4.1±0.6	*0.74*	*0.36*	*0.76*
% of deep sleep	19.8±1.6	18.5±1.5	19.7±1.4	*0.73*	*0.95*	*0.84*
Wake after sleep onset (min)	40.7±9.5	42.2±7.6	39.5±6.1	*0.81*	*0.40*	*0.77*
% Stage 1 sleep	5.3±1.2	5.3±0.9	5.6±1.1	*0.86*	*0.76*	*0.64*

AHI=apnea hypopnea index. AI=apnea index. TST=total sleep time. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus. Shaded are p-values <0.05. Standard error of the means are shown.

The device attached in OFF modus did not have a significant effect on the desaturation index when compared to no device. The device in ON modus did have a significant effect on the desaturation index when compared to no device and in OFF modus (Table 2).

Mean total sleep times were 436 (ND), 417 (DOFF) and 393 (DON) minutes (p=0.14, 0.00, 0.13), showing that the device in ON modus lead to a significant reduction in total sleep time when compared to no device attached.

Arousal index was found to be 9.0 (ND), 9.9 (DOFF) and 6.8 (DON) (p=0.77, 0.04, 0.01). The arousal index was significantly lower in the group with the device in ON modus when compared to the no device group and the group with the device in OFF modus.

The effect of the device and its status on mean oxygen saturation, sleep efficiency, percentage of deep sleep and number of awakenings was insignificant. Sleep efficiency was found to be 91.9% (ND), 89.9% (DOFF) and 88.3% (DON) (p= 0.21, 0.10, 0.59), percentage of deep sleep

was 19.8 (ND), 18.5 (DOFF) and 19.7 (DON) (p= 0.73, 0.95, 0.84). Mean number of awakenings was 3.4 (ND), 3.9 (DOFF) and 4.1 (DON) (p=0.74, 0.36, 0.76).

Figure 2A Effect of device on AHI

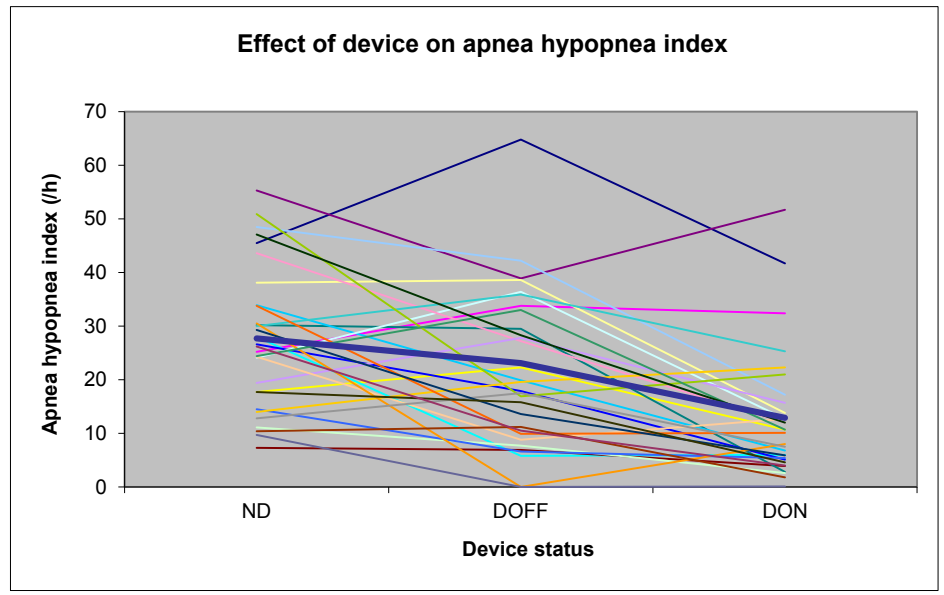


Figure 2B Effect of device on supine AHI

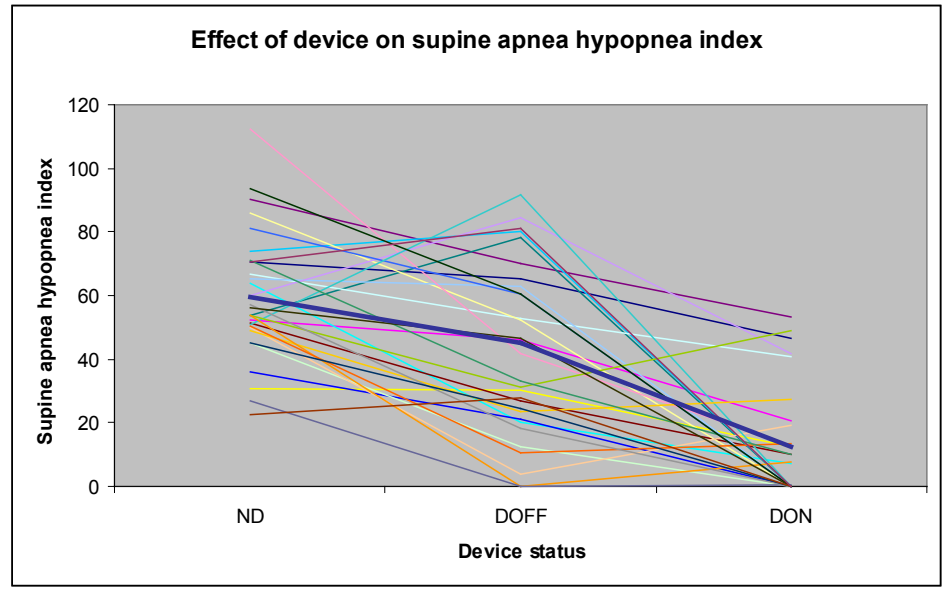
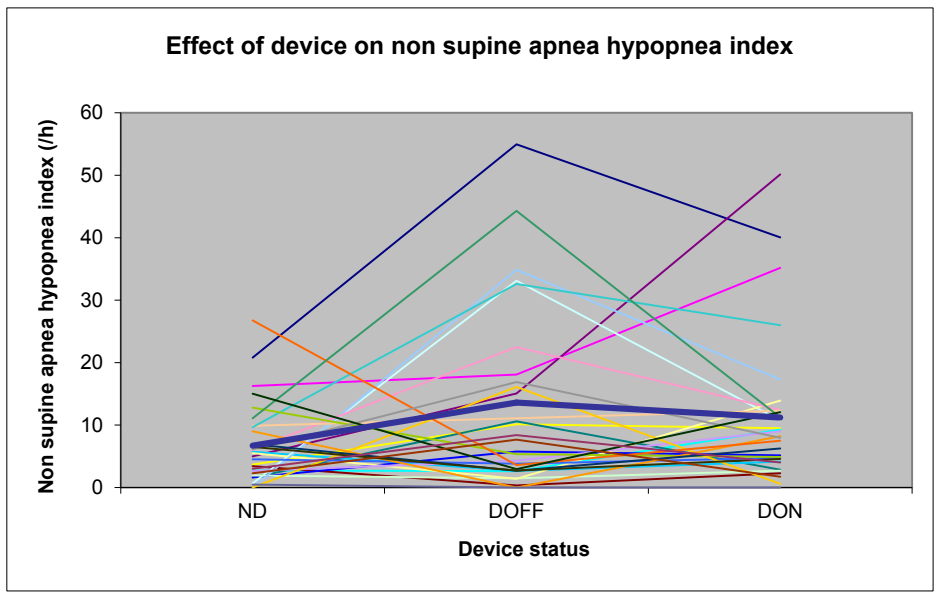


Figure 2C Effect of device on non supine AHI



2A, B, C: The thickened line depicts the mean value. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus.

Figure 3A Effect of device on AHI (group of patients with device ON during first night)

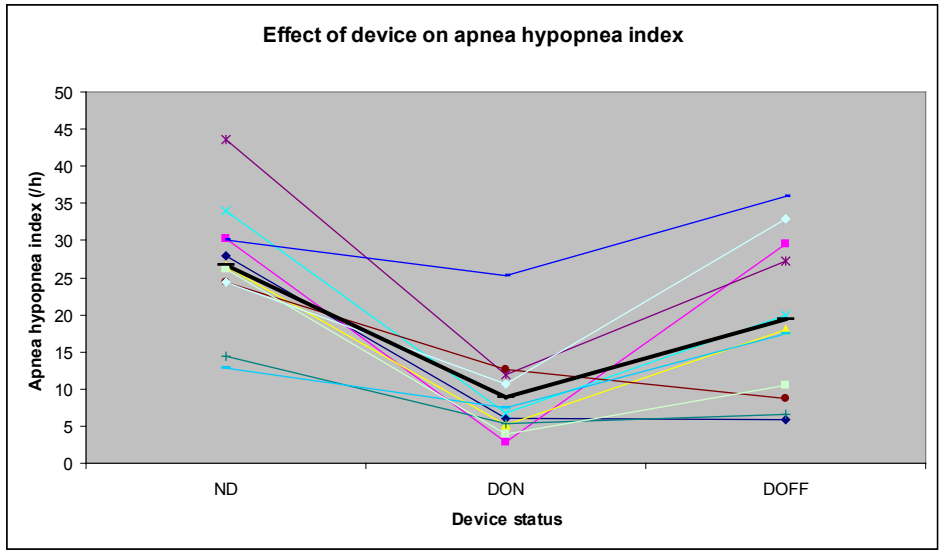
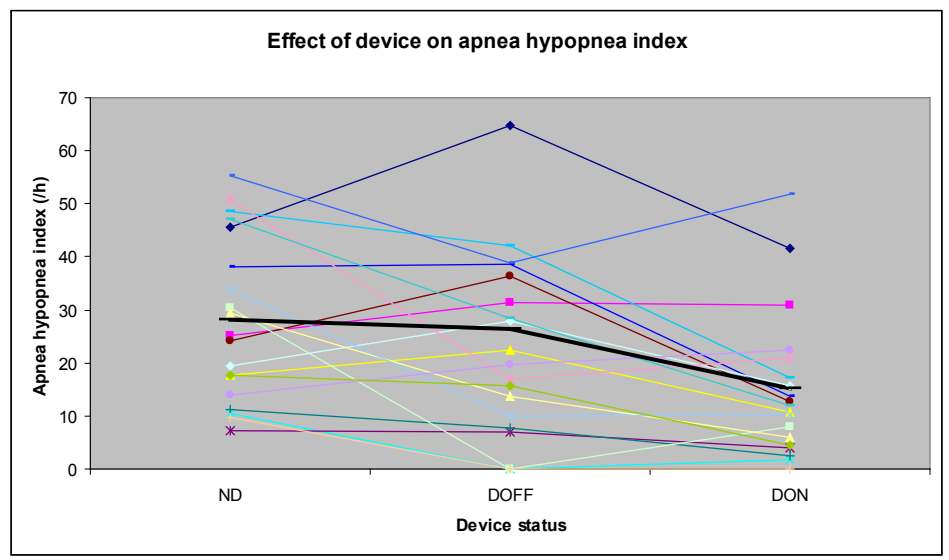
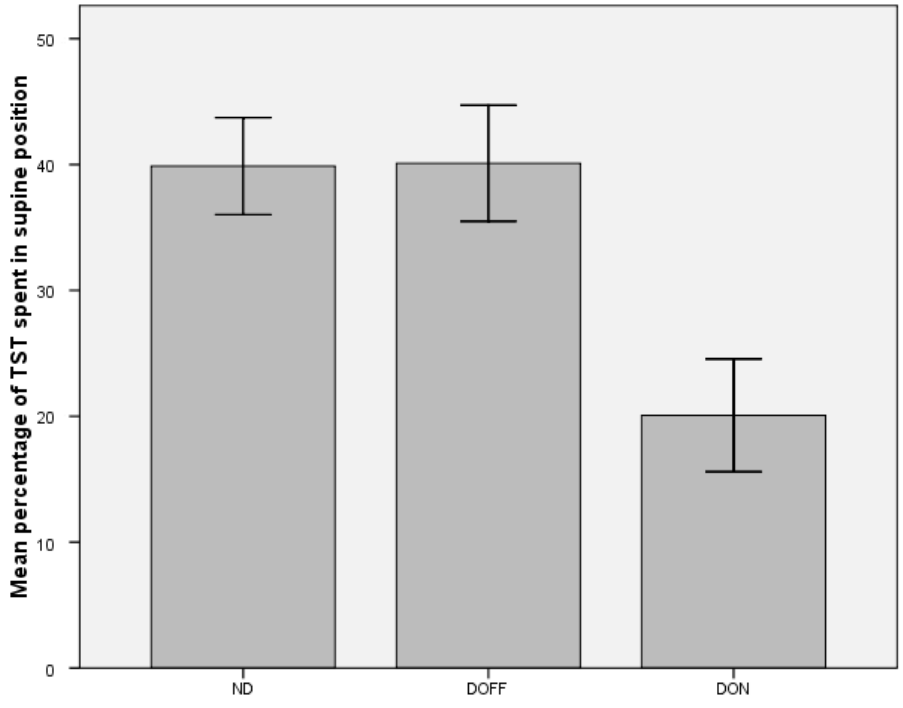


Figure 3B Effect of device on AHI (group of patients with device OFF during first night)



3A,B: The thickened line depicts the mean value. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus.

Figure 4 Effect of device on percentage of TST in supine position



TST=total sleep time. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus. The y error bars depict the standard error of the mean.

Discussion

56% of sleep apnea patients suffer from position dependent OSAS (POSAS), with position dependency defined as an at least two times higher AHI in supine position than the mean AHI in the other positions and a percentage of total sleep time in supine position ≥ 10% and ≤ 90%.[19,23] Although the finding that sleep apnea is often positional dependent is not new, remarkably few attempts have been reported to treat sleep apnea by influencing sleep position. Positional therapy can be defined as preventing patients to sleep in the worst sleeping position. The worst sleeping position is usually but not always the supine position. Previous attempts by strapping an object on the back (tennis balls, squash balls, special vests[24-27], "shark fins" etc) were unsuccessful due to arousals whilst turning from one lateral position to the other, thereby disturbing sleep architecture and sleep quality. This leads to serious lack of compliance. Tennis ball therapy, for example, has a long term compliance of less than 10%, mainly because of its effect on sleep quality and comfort complaints.[26]

The present device gets around this problem, since this small, light and comfortable to wear device does not cause any discomfort during position change.

Permut et al. recently showed that positional therapy with a bulky mass strapped to the back was equal to CPAP in normalizing the AHI in patients with a mild to moderate POSAS. [29] However, patient selection criteria and thus definition of POSAS were not the same as in our study. In their proposal for an alternative definition of POSAS, patients should have a non-supine AHI of <5. We believe this definition of POSAS to be too restrictive, because a significant number of patients with position dependent obstructive sleep apnea would be excluded, whilst using positional therapy in these patients could lead to a clinical significant lowering of the AHI. So unlike the group of Permut, we did include patients suffering from severe POSAS with AHI >5 in lateral sleeping position. This explains that our mean AHI was 12.8 and not below 5.

When Sher's AHI definition of surgical success (AHI<20 and >50% reduction of AHI) is used a 60.0% (18/30) success rate is achieved.[30] This success rate would have been even higher (66.6%) if the three patients in which the device did not work properly due to technical failure were not taken into account. In 7 out of 30 or 27(23-26%)) patients the overall AHI dropped below 5 when using the device in ON modus, whereas using the device in OFF modus did not cause the AHI to drop below 5.

Wearing the device in ON modus had a significant effect on AHI when compared to wearing no device (P=0.00). When worn in OFF modus however the device also had a significant effect on AHI when compared to wearing no device (p=0.04). This could be because subjects felt the device in their neck, shifting the preferred position of the head without leading to clear changes in other sleep parameters.

Apnea hypopnea index, apnea index and desaturation index usually increase during REM sleep. So longer periods of REM sleep would lead to higher index values. However, no significant differences in REM sleep percentages of total sleep time, nor AHI during REM sleep were found between ND, DOFF and DON group.

The effect of wearing or not wearing the device and its status on sleep efficiency, percentage of deep sleep and number of awakenings was insignificant. There was however, a significant shortening of the mean total sleep time in the DON modus compared to the ND. Other sleep quality items were not different between groups, except for the arousal index. This was significantly reduced in the DON, implying that the arousals evoked by the device outweigh the arousals caused by the otherwise occurring apneas and hypopneas. Since validated post-PSG quality of sleep questionnaires do not exist we did not investigate this any further, therefore interpretation of the sleep time shortening in the DON modus is difficult.

Since overnight AHI and sleep quality were our primary endpoints of the study we did not further analyse how often stimulator activity led to position change and either an arousal or awakening. Another limitation of this study is the lack of subjective data. The initial setup of this study was to have patients fill in Epworth Sleepiness Scales following each night in hospital and ask them about their experiences with the device and their subjective sleep quality. Unfortunately, at the end of the study period we noticed that a considerable number of patients had not received the questionnaire.

The average percentage of total sleep time spent in supine position significantly changed from 40% to 19%. The data analysis was performed on intention to treat basis. The relatively high residual percentage of supine sleeping position is mostly due to the three patients in whom the device did not work properly. The median percentage supine sleeping position was found to be 5% (data not shown). This indicates that with technical improvements in the next generation of the device it is realistic to believe that a much lower mean percentage supine sleeping position can be achieved. The second reason it did not decrease to 0% could be because of a discrepancy between the two separate position recording sensors. The position sensor in the device was in the neck, the PSG position sensor was attached to

the midline of the abdominal wall. In some subjects obstructive episodes might be alleved through mere rotation of the head sideways while the trunk remained in the supine position. The finding that the occurrence of obstructive sleep apnea not solely depends on position of the trunk but also depends on the position of the head has been discussed in more detail elsewhere.[31] Also, the extent to which participants respond to the stimulus to change their body position might be different, depending on their response threshold. That is to say, the higher their response threshold, the longer the TST in supine position, indicating our stimulus might have been too weak for some of the patients. Future research in our hospital is ongoing and concentrating on collecting subjective results and offering different stimuli to be able to decrease the percentage of total sleep time spent in supine position and thereby the overall AHI.

The results of the present study are very convincing and the impact on future treatment of sleep apnea could be enormous. In approximately 80% of patients sleeping position plays a role (56 % with a factor 2 difference in AHI, the rest with less than factor 2). We expect that positional therapy with such a device can be applied as single treatment in many patients with mild to moderate position dependent obstructive sleep apnea, while in patients with a more severe obstructive sleep apnea such a device could be used in combination with other treatment modalities. Also many patients with central sleep apnea syndrome might benefit from this simple, cheap and successful treatment.[32,33] Further research with a technically improved device is ongoing.

References

1. Flemons WW (2002) Clinical practice. Obstructive sleep apnea. N Engl J Med 347:498-504.
2. Young T, Palta M, Dempsey J, Skatrud J, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328:1230-5.
3. Young T, Evans L, Finn L, Palta M (1997) Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 20:705-6.
4. Shamsuzzaman ASM, Gersh BJ, Somers VK (2003) Obstructive sleep apnea, implications for cardiac and vascular disease. JAMA 290:1906-14.
5. Phillipson EA. Sleep apnea-a major public health problem (1993) N Engl J Med 328:1271-3.
6. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM (2001) Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health study. Am J RespirCrit Care Med 163:19-25.
7. Marin JM, Carrizo SJ, Vicente E, Agusti AG (2005) Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 365:1046-53.
8. Dyken ME, Somers VK, Yamada T, Ren ZY, Zimmerman MB (1996) Investigating the relationship between stroke and obstructive sleep apnea. Stroke 27:401-7.
9. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342:1378-84.
10. George CF, Smiley A (1999) Sleep apnea and automobile crashes. Sleep 22:790-5.
11. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18:501-10.
12. Jenkinson C, Davies RJ, Mullins R, Stradling JR (1999) Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet 353:2100-5.
13. Richard W, Venker W, den Herder C, Kox D, van den Berg B, Laman M, van Tinteren H, de Vries N (2007) Acceptance and long-term compliance of nCPAP in obstructive sleep apnea. Eur Arch Otorhinolaryngol 264:1081-6.
14. Ravesloot MJL, de Vries N (2011) Reliable calculation of the efficacy of non-surgical and surgical treatment of obstructive sleep apnea revisited. Sleep 34:105-10.
15. Petit F, Pepin J, Bettega G, Sadek H, Raphael B, Levy P (2002) Mandibular advancement devices: rate of contraindications in 100 consecutive obstructive sleep apnea patients. Am J Respir Crit Care Med 166:274-278.
16. Cartwright RD (1984) Effect of sleep position on sleep apnea severity. Sleep 7:110-4.
17. George CF, Millar TW, Kryger MH (1988) Sleep apnea and body position during sleep. Sleep 11:90-9.
18. Cartwright RD, Diaz F, Lloyd S (1991) The effect of sleep posture and sleep stage on apnea frequency. Sleep 14:351-3.
19. Oksenberg A, Silverberg DS, Arons E, Radwan H (1997) Positional vsnonpositional obstructive sleep apnea patients. Chest 112:629-39.

20. Oksenberg A, Khamaysi I, Silverberg DS, Tarasiuk A (2000) Association of body position with severity of apneic events in patients with severe nonpositional obstructive sleep apnea. Chest 118:1018-24.

21. Itasaka Y, Miyazaki S, Ishikawa K, Togawa K (2000) The influence of sleep position and obesity on sleep apnea. Psychiatry Clin Neurosci 54:340-1.

22. Akita Y, Kawakatsu K, Hattori C, Hattori H, Suzuki K, Nishimura T (2003) Posture of patients with sleep apnea during sleep. Acta Otolaryngol Suppl 550:41-5.

23. Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N (2006) The role of sleeping position in obstructive sleep apnea. Eur Arch Otorhinolaryngol 263:946-50.

24. Maurer JT, Stuck BA, Hein G, Verse T, Hörmann K (2003) Schlafapnoetherapie mit einer neuartigen rückenlage-verhinderungs-weste. Dtsch Med Wochenschr 128:71-5.

25. Wenzel S, Smith E, Leiacker R, Fischer Y (2007) Efficacy and longterm compliance of the vest preventing the supine position in patients with obstructive sleep apnea. Laryngorhinootologie 86:579-83.

26. Bignold JJ, Deans-Costi G, Goldsworthy MR, Robertson CA, McEvoy D, Catcheside PG, Mercer JD (2009) Poor long-term patient compliance with the tennis ball technique for treating positional obstructive sleep apnea. J Clin Sleep Med 5:428-30.

27. Oksenberg A, Silverberg D, Offenbach D, Arons E (2006) Positional therapy for obstructive sleep apnea patients: A 6-month follow-up study. Laryngoscope 116:1995-2000.

28. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research (1999) The report of an American academy of sleep medicine task force. Sleep 22:667-89.

29. Permut I, Diaz-Abad M, Chatila W, Crocetti J, Gaughan JP, D'Alonzo GE, Krachman SL (2010) Comparison of positional therapy to CPAP in patients with positional obstructive sleep apnea. J Clin Sleep Med 6:238-43.

30. Sher AE, Schechtman KB, Piccirillo JF (1996) The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 19:156-77.

31. Van Kesteren ER, van Maanen JP, Hilgevoord AAJ, Laman DM, de Vries N (2011) Quantitative effects of trunk and head position on the apnea hypopnea index in obstructive sleep apnea. Sleep 34:1075-81.

32. Joho S, Oda Y, Hirai T, Inoue H (2010) Impact of sleeping position on central sleep apnea/ Cheyne-Stokes respiration in patients with heart failure. Sleep med 11:143-8.

33. Szollosi I, Roebuck T, Thompson B, Naughton MT (2006) Lateral sleeping position reduces severity of central sleep apnea / Cheyne-Stokes respiration. Sleep 29:1045-51.

chapter 5

ONE STAGE MULTILEVEL SURGERY (UVULOPALATOPHARYNGOPLASTY, HYOID SUSPENSION, RADIOFREQUENT ABLATION OF THE TONGUE BASE WITH/WITHOUT GENIOGLOSSUS ADVANCEMENT), IN OBSTRUCTIVE SLEEP APNEA SYNDROME

Wietske Richard, Dennis Kox, Cindy den Herder, Harm van Tinteren, Nico de Vries

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Abstract

We evaluated the surgical results of a one tempo multilevel surgical approach of the upper airway to treat patients with obstructive sleep apnea syndrome (OSAS) in a prospective case series. Twenty-two patients with OSAS and obstruction at both palatinal and tongue base level, as assessed by sleep endoscopy, underwent UPPP, RFTB, HS with or without GA in one operative session. The mean apnea hypopnea index (AHI) decreased from 48.7 (range 17.4-100.9) to 28.8 (P<0.0001). The success rate (AHI <20 and >50% reduction in AHI) was 45%, the response rate (reduction in AHI of 20-50%) was 27%. The overall response rate was 72%. The success rates of patients with an AHI <55 and >55 were 56 and 0%, respectively. The overall response rate of patients with an AHI <55 was 78% and >55 was 50%. Improvement of desaturation index was significant from 31.9 to 17.6 (P<0.0001). Visual Analogue Scales for snoring and hypersomnolence and the Epworth Sleepiness Scores showed significant improvements too (all P<0.0001). There was no difference in objective and subjective outcomes between the group with and without GA. This study demonstrates that one stage multilevel surgery, in which genioglossus advancement is not of additional value, is a valuable addition to the therapeutic armentarium and can be considered a viable alternative, objective as well as subjective, to NCPAP or as primary treatment in well selected patients with moderate to severe OSAS with an AHI <55.

Key words. Multilevel surgery - Sleep apnea syndrome - CPAP-therapy

Introduction

Obstructive sleep apnea syndrome (OSAS) is very frequent and increasingly recognized as a major health problem.[1] In severe OSAS, morbidity and mortality from cardiovascular disease are increased if left untreated: increased risks of developing hypertension, myocardial infarction and cerebrovascular disease respectively, has been reported.[2-4] The risk to be involved in traffic accidents is increased in case AHI > 40,[5] while headache, impotence, cognitive impairment and depression often occur.

Treatment of OSAS consists of lifestyle alterations, as weight reduction in case of overweight, and abstinence of alcohol, sedatives and sleep medication. Non-invasive treatment consists of the use of a mandibular repositioning appliance (MRA) in mild to moderate OSAS,[6] and nasal continuous positive airway pressure (NCPAP) in moderate to severe OSAS.[7,8] NCPAP, which acts as an pneumatic splint, is regarded as gold standard therapy for severe OSAS. Unfortunately, compliance of and adherence to this treatment is poor, up to 50% of patients can not accept NCPAP therapy or refuses its treatment upfront.[9-15]

Since treatment remains indicated in severe OSAS with NCPAP failure, several invasive alternatives are being explored. Surgical interventions are available, such as uvulopalatopharyngoplasty (UPPP) and variations of it, in case of palatinal obstruction, and hyoid suspension (HS) and genioglossus advancement (GA), in retrolingual obstruction and maxillomandibular advancement or tracheostomy. In addition, minimally invasive interventions exist, such as radiofrequent thermotherapy (RFTT) of palate and/or tongue base. Surgery can be divided in unilevel (at palatinal or tongue base level only) and multilevel (surgery at both these levels), and can be performed either staged, or in one surgical tempo.

In increasing severity of OSAS, the likelihood that obstruction is present on both palatinal as well as retrolingual level is high. This is confirmed by sleep endoscopy of large series of patients with OSAS indeed showing retropalatinal as well as retrolingual obstruction of the upper airway in a large percentage of cases.[16] Therefore unilevel surgery is often disappointing. A therapeutic dilemma is whether these patients should undergo intervention at both levels staged (and in which sequence) or simultaneously. Performing multilevel surgery in a staged sequence will in cases of multilevel obstruction often lead to a prolonged path to success. In this paper, we present our results of one tempo multilevel surgery in OSAS and NCPAP failure or refusal.

Patients and methods

All patients who visited our department from July 2003 to June 2005 because of habitual snoring and/or suspicion of sleep apnea syndrome were evaluated by history, physical examination, full overnight polysomnography and either by midazolam or propofol induced sedated endoscopy. Patients with moderate to severe OSAS, both retrolingual and retropalatinal narrowing or collapse and refusal or non-acceptance of NCPAP treatment were advised a multilevel surgical approach.

Apneas were defined as cessation of oronasal airflow for at least 10 s. Hypopneas were defined as periods of reduction of >30% oronasal airflow during minimally 10 s. The AHI is the mean number of apneas and hypopneas per hour of sleep, and signifies the severity of OSAS. Mild OSAS: AHI ≥5 and < 15, moderate OSAS: AHI ≥ 15 and < 30 and severe OSAS: AHI ≥ 30.[17] The desaturation index is defined as the mean number of desaturations of >4% per hour. Full overnight polysomnography was repeated 2-10 months (mean: 4,4 months) postoperatively. To compare hypersomnolence during daytime and snoring complaints pre- and postoperatively, we used a visual analogue scoring system (VAS) and the Epworth Sleepiness Scale (ESS).

The body mass index (BMI), a rank for obesity and important criterion for OSAS, was calculated by dividing weight (kg) by the square of length (m^2).

Surgical success was defined as AHI <20 and >50% reduction in AHI and response rate as reduction of AHI between 20 and 50%. The overall response rate was defined as more than 20% reduction in AHI.

Treating obstruction at palatinal level

Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty was performed according to Fujita's technique; the anterior and posterior tonsillar pillars were trimmed and reoriented, and the uvula was excised to create more space retropalatinal.[18] Tonsillectomy was performed if it had not been done previously (in 15 of 22 (68%) patients).

Treating obstruction at tongue base level

Radiofrequent ablation of the tongue base (Celon®)

Radiofrequent ablation of the tongue base (Celon®) was used to accomplish stiffening and volume reduction of the base of the tongue. Energy was delivered with an exclusive needle

device through the dorsal surface of the tongue. Evidence based criteria for technical adjustment and optimal energy dosage according to relevant increase in lesion size were used.[19,20] After the initial surgical procedure, on indication additional RFTB was performed. According to Stuck et al. about 600 J appears to be the ideal adjustment for energy delivery.[19] During the multilevel operation session at 6 lesions sides ± 42 J was delivered (±252 J). A total of 15 patients received additional RFTB therapy under local anaesthesia to reach the maximal lesion size. To reduce the risk of swelling of the tongue we did not administer 600 J directly in the multilevel session.

Hyoid suspension

After exposure via an external horizontal incision at the level of the membrana thyrohyoidea, the strap muscles (M. sternohyoideus, M. omohyoideus and en M. thyrohyoideus) were divided just below the hyoid and superior to the hyoid the tendon of the M. stylohyoideus was divided from the hyoid bone. Mobilising the hyoid bone in anterocaudal direction and fixing it permanently to the thyroid cartilage created more space retrolingually.[21]

Genioglossus advancement.

A standard anterior mandibular osteotomy, limited to advancement of a rectangular window of the mandible including the genial tubercle and genioglossus musculature, but without rotation of the segment, was performed.[22] The outer cortex and medulla were removed, the lingual cortical plate advanced and fixed with bone screws. The decision to add the GA to the surgery was part of our temporally standard treatment.

Per- and postoperative care

Conscientious monitoring of oxygen saturations at an Intensive Care Unit for one night after surgery was regarded mandatory because of the risk of a compromised airway due to postoperative bleeding or oedema. All patients received 2 g of amoxicillin i.v. during surgery and 3 dd 625 mg orally during one week postoperatively. Oral painkillers were administered only when necessary. Steroids were not used routinely. Patients were usually dismissed 48 to 72 h postoperatively.

Statistics

Changes in parameters before and after intervention were compared by means of a Wilcoxon Signed Rank Test (paired analyses). Differences in parameters between interventions (with or without genioglossus advancement) were tested with a Wilcoxon Rank Sum Test. For the binomial proportions (responses) exact 95% confidence intervals were calculated.

Results

Twenty-two patients underwent multilevel surgery, 14 with genioglossus advancement and 8 without. Patient characteristics are shown in Table 1. Between the group with and without genioglossus advancement, there were no significant preoperative differences in AHI, desaturation index (DI), BMI, total sleeping time (TST), ESS and VAS scores. Also in treatment outcome there were no significant differences (Table 2).

Table 1 Baseline characteristics

Measurement	Total subjects *(N=22)*
Age (year)	50.3 ± 7.7
BMI (kg/m^2)	27.7 ± 3.4
AHI	48.7 ± 19.7
Ratio male : female	20 : 2

BMI: body mass index; AHI: apnea hypopnea index.

Table 2 P-values for differences in preoperative characteristics and treatment outcome between group with and without genioglossal advancement.

Variable	*P*-value baseline characteristics	*P*-value treatment outcome
AHI	0.6859	1.0000
DI	0.1236	0.0498*
TST	0.4994	0.9715
BMI	0.4423	0.5560
VAS snurk	1.0000	0.6821
VAS hyps	0.4071	1.0000
ESS	0.7124	0.5779

** Borderline significancy*

The mean AHI for the total group decreased significantly from 48.7 (range 17.4-100.9) to 28.8 (diff 19.9 SD 18.5 *P*<0.0001). Surgical success, defined as AHI <20 and >50% reduction in AHI, was seen in 45% (95% CI 24-68%) of patients. Reduction of AHI between 20 and 50%, response rate, was seen in 16 patients (27%). The overall response rate was 72% (95% CI 49-89).

Dividing patients in three groups on the basis of the AHI, the success rates decreased with increasing AHI (Table 3). The success rates of patients with an AHI <55 and >55 were 56 and 0%, respectively. Overall, four patients increased in AHI after surgery. The AHI in supine position decreased significantly from 63.3 to 35.6 (*P*=0.0055). The desaturation index (DI) decreased from 31.9 to 17.6 (*P*<0.0001). In 83% of the patients without surgical success the DI did decrease. In Figs. 1 and 2 the relative differences in AHI and DI pre- and post surgery for each patient are shown, respectively.

Table 3 Success rates on basis of the AHI

N	AHI	Success rate (%)
4	<40	60
13	40-55	53,8
4	>55	0

Figure 1 Relative difference in AHI pre- and post surgery

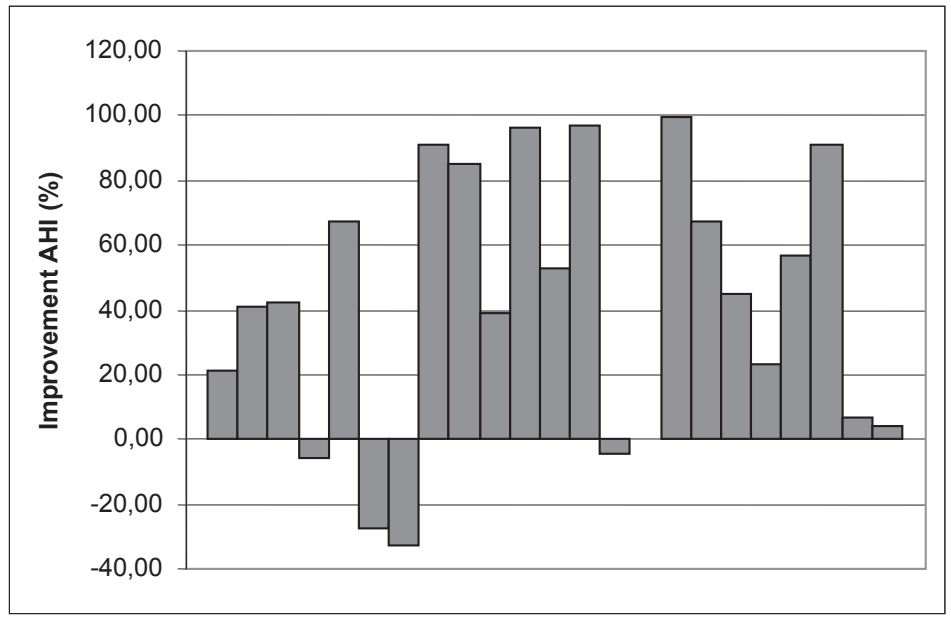
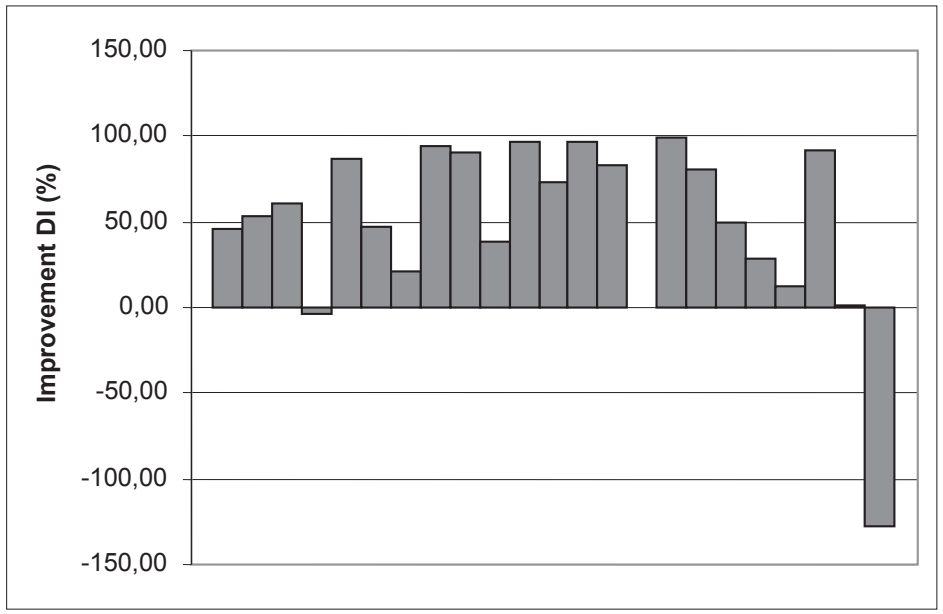


Figure 2 Relative difference in DI pre- and post surgery



We did not see differences in pre operative BMI (range 23.8-39) between the successful group and the non-successful group. BMI and total sleep time (TST) did not change substantially before and after surgery (respectively, *P*=0.2292 and *P*=0.3855).

Hypersomnolence during daytime and snoring complaints pre- and postoperatively decreased from 8.6 to 3.6 (*P*<0.0001) and 8.6 to 3.8 (*P*<0.0001) respectively. The ESS improved significantly from 7.4 to 3.9 (*P*<0.0001).

Complications

We did not encounter infection, postoperative haemorrhage, tongue base abscess, compromised airway, or velopharyngeal insufficiency postoperatively. Only one serious complication was seen; a long-lasting hypoglossal nerve paresis, believed to be caused by the sutures used for the hyoid suspension. Electromyography presently shows signs of reinnervation.

Discussion

A variety of interventions, both minimally invasive (RFTT of palate and tongue base) and surgical (UPPP, laser glossectomy (LG), HS, GA) have been reported as part of multilevel treatment in severe OSAS and NCPAP failure or non-acceptance, both staged and in one session.[23-44] We decided to perform multilevel surgery in an one tempo procedure. In a staged surgical procedure, patients are more prone to become discouraged in completing the advised treatment and will be treated only partly.

The application of this surgical approach has resulted in a success rate of 45% and overall response rate of 72%. Table 4 shows data of reported one stage multilevel surgical interventions, with success rates of 42-78% and overall response rates to approximately 73%.[36-44] Differences in success rates are probably due to variations in study design and patient selection. The severity of OSAS preoperatively differs between the studies. In some studies also patients with mild OSAS (AHI >5) are included. The chance of surgical success is inversely related to the AHI: the higher the AHI preoperatively, the lower the success rate (Table 3).[36,39-42] Also the definition of success is different between the studies whereas in some studies patients are included who already preoperatively met the criteria.

Table 4 Reported series on one stage multilevel surgery, excluding MMA

Authors	Procedure	N	AHI pre	AHI post	Success rate (%)	Response rate (%)	BMI
Riley et al	UPPP, HS, GA,	223	48.3	9.5	60	?	29.2
Lee et al	UPPP, GA	35	53	19	69	?	?
Hsu and Brett	UPPP, HS, GA	13	52.8	15.6	76.9	?	31
Hendler et al	UPPP, GA	33	60.2	28.8	45.5	72.7	32.6
Neruntarat	UPPP, HS, GA	46	47.9	18.6	65.2	?	27.1
Verse et al	UPPP, HS	31	40.8	25.8	41.9	?	28.5
Miller et al	UPPP, GA, ± HS	24	52.9	15.9	67	?	30.5
Datillo and Drooger	UPPP, HS, GA	42	36.5	14.5	78	?	?
Hörmann et al	UPPP, HS RFTB	66	38.9	19.3	57.6	?	28
Present series	UPPP, HS, RFTB ± GA	22	48.7	28.8	45	72	27.7

Success rate was defined as a reduction of AHI >50% and AHI <20 or equal with CPAP in Riley et al, as a reduction of AHI >50% and/or AHI <20 in Hsu and Brett, as a reduction of AHI >50% and AHI <20 in Hendler et al, Neruntarat et al, Miller et al and Hörmann et al, as AHI < 20 in Lee et al, as a reduction of AHI >50% and AHI< 15 in Verse et al and as a reduction of AHI >50% or AHI< 15 in Datillo and Drooger. ***Responders*** are defined as reduction of AHI >50% in Hendler et al and as reduction of AHI> 20 in Hörmann et al.

UPPP: uvulopalatopharyngoplasty, HS: hyoid suspension, GA: genioglossal advancement, MLG: midline laser glossectomy, RFTB: radiofrequent ablation tongue base, MMA: maxillomandibular advancement

For the patients in this study NCPAP therapy is no longer an option. Still, an alternative treatment is indicated and also a response (AHI reduction of 20-50%) is of significant value both in terms of increased quality of life as in terms of reduction in risk of morbidity and mortality. The real AHI threshold below which apnea severity becomes inconsequential has still to be determined. The increased morbidity and mortality of OSAS reported in literature is based on limited data. Apart from the evidence of an increased risk to be involved in car crashes in AHI levels above 40, there is still need for more evidence.[2,5]

In our sample, the AHI of four patients increased after intervention. It is known that 56% of patients with sleep apnea syndrome are position dependant.[45,46] Two of these four patients were positional and slept more in supine position postoperatively. Another patient had a substantial weight gain of 4%, which may explain the postoperative higher AHI. A 10% weight gain predict an approximate 32% increase in the AHI.[47] The fourth patient started with an AHI of 73. When the success rate was evaluated according to the severity based on preoperative AHI, there was a clear trend. No patients with an AHI >55 met the criteria for success. Not yet understood skeletal and soft tissue deficiencies with subsequent changes in aerodynamic properties after intervention results in non-response to reconstruction of the upper airway. In these patients maxillomandibular advancement (MMA [25,30,36,39,43,48,49]) upfront, with tracheotomy in reserve as last refuge, may be preferred above multilevel surgery. The invasiveness of these modalities with significant morbidity and potential side effects indicates that these procedures should be kept for patients with an AHI above 55 as primary surgical treatment, and for non-responders to multilevel surgery with an AHI <55.

We conclude that one stage multilevel surgery, in which genioglossus advancement is probably not of additional value, is a valuable addition to the therapeutic armentarium and can be considered a viable alternative, objective as well as subjective, to NCPAP or as primary treatment in well selected patients with moderate to severe OSAS with an AHI <55.

References

1. Flemons WW (2002) Clinical practice. Obstructive sleep apnea. N Engl J Med 347(7):498-504
2. Shamsuzzaman ASM, Gersh BJ, Somers VK (2003) Obstructive sleep apnea, implications for cardiac and vascular disease. JAMA 290(14):1906-14
3. Partinen M, Guilleminault C (1990) Daytime sleepiness and vascular morbidity at seven year follow-up in obstructive sleep apnea patients. Chest 97:27-32
4. He J, Kryger MH, Zorick FJ, Conway W, Roth T (1988) Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest 94(1):9-14
5. George CF, Smiley A (1999) Sleep apnea and automobile crashes. Sleep 22:790-5
6. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18(6):501-10
7. Jenkinson C, Davies RJ, Mullins R, Stradling JR (1999) Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet 353(9170):2100-5
8. (1994) Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Am J Crit Care Med 150:1738-45
9. Grunstein RR (1995) Nasal continuous positive airway pressure treatment for obstructive sleep apnoea. Thorax 50(10):1106-13
10. Fleury B, Rakotonanahary D, Tehindrazanarivelo AD, Hausser-Hauw C, Lebeau B (1994) Long-term compliance to continuous positive airway pressure therapy (nCPAP) set up during a split–night polysomnography. Sleep 17(6):512-5
11. Strollo PJ Jr, Sanders MH, Costantino JP, Walsh SK, Stiller RA, Atwood CW Jr (1996) Split–night studies for the diagnosis and treatment of sleep-disordered breathing. Sleep 19(10 Suppl):S255-9
12. Rauscher H, Popp W, Wanke T, Zwick H (1991) Acceptance of CPAP therapy for sleep apnea. Chest 100(4):1019-23
13. Hoffstein V, Viner S, Mateika S, Conway J (1992) Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis 145:841-5
14. Reeves-Hoche MK, Meck R, Zwillich CW (1994) Nasal CPAP: an objective evaluation of patient compliance. Am J Respir Crit Care Med 149(1):149-54
15. Meurice JC, Dore P, Paquereau J, Neau JP, Ingrand P, Chavagnat JJ, Patte F (1994) Predictive factors of long term compliance with nasal continuous positive airway pressure treatment in sleep apnea syndrome. Chest 105(2):429-33
16. Hessel NS, de Vries N (2002) Diagnostic work-up of socially unacceptable snoring. II. Sleep endoscopy. Eur Arch Otorhinolaryngol 259(3):158-61
17. (1999) Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American academy of sleep medicine task force. Sleep 22(5):667-89

18. Fujita S, Conway W, Zorick F, Roth T (1981) Surgical corrections of anatomical abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 89:923-34

19. Stuck BA, Köpke J, Maurer JT, Verse T, Eckert A, Bran G, Duber C, Hormann K (2003) Lesion formation in radio frequency surgery of the tongue base. Laryngoscope 113:1572-6

20. Den Herder C, Kox D, van Tinteren H, de Vries N. (2006) Bipolar radiofrequency induced thermotherapy of the tongue base: its complications, acceptance and effectiveness under local anesthesia. Eur Arch Otorhinolaryngol 263(11):1031-40

21. Riley RW, Powell NB, Guilleminault C (1994) Obstructive sleep apnea and the hyoid: a revised surgical procedure. Otolaryngol Head Neck Surg 111(6):717-21

22. Kerner MM, Hale RG, Silva Kim (2002) A novel three-piece anterior mandibular visor osteotomyfor genioglossus advancement in surgery for obstructive sleep apnea. Oper Techn Otolaryngol Head Neck Surg 13(2);175-7

23. Riley RW, Powell NB, Guilleminault C (1986) Inferior sagittal osteotomy of the mandible with hyoid myotomy-suspension: a new procedure for obstructive sleep apnea.. Otolaryngol Head Neck Surg 94(5):589-93

24. 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(2):159-64

25. Riley RW, Powell NB, Guilleminault C (1993) Obstructive sleep apnea syndrome: a surgical protocol for dynamic upper airway reconstruction. J Oral Maxillofac Surg 51(7):742-7; discussion 748-9

26. Johnson NT, Chinn J (1994) Uulopalato-pharyngoplasty and inferior sagittal mandibular osteotomy with genioglossus advancement for treatment of obstructive sleep apnea. Chest 105:278-83

27. Ramirez SG, Loube DI (1996) Inferior sagittal osteotomy with hyoid bone suspension for obese patients with sleep apnea. Arch Otolaryngol Head Neck Surg 122(9):953-7

28. Elasfour A, Miyazaki S, Itasaka Y, Yamakawa K, Ishikawa K, Togawa K (1998) Evaluation of uvulopharyngoplasty in treatment of obstructive sleep apnea syndrome. Acta Otolaryngol Suppl 537:52-6

29. Li KK, Powell NB, Riley RW, Troell R, Guilleminault C (1999) Overview of phase I surgery for obstructive sleep apnea syndrome. Ear Nose Throat J 78(11):836-7, 841-5

30. Li KK, Riley RW, Powell NB, Troell R, Guilleminault C (1999) Overview of phase II surgery for obstructive sleep apnea syndrome. Ear Nose Throat J 78(11): 851, 854-7

31. Bettega G, Pepin JL, Veale D, Deschaux C, Raphael B, Levy P (2000) Obstructive sleep apnea syndrome. Fifty-one consecutive patients treated by maxillofacial surgery. Am J respire Crit Care Med 162:641-9

32. Hörmann K, Hirth K, Erhardt T, Maurer JT, Verse T (2001) Modified hyoid suspension for therapy of sleep related breathing disorders. Operative technique and complications. Laryngorhinootologie 80(9):517-21

33. Vilaseca I, Morello A, Monserrat JM, Santamaria J, Iranzo A (2002) Usefulness of uvulopalatopharyngoplasty with genioglossus and hyoid advancement in the treatment of obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 128:435-40

34. Bowden MT, Kezirian EJ, Utley D, Goode RL (2005) Outcomes of hyoid suspension for the treatment of obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 131(5):440-5

35. Den Herder C, van Tinteren H, de Vries N (2005) Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. Laryngoscope 115(4):740-5

36. Riley RW, Powell NB, Guilleminault C (1993) Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. Otolaryngol Head Neck Surg 108(2):117-25

37. Lee NR, Givens CD, Wilson J, Robins RB (1999) Staged surgical treatment of obstructive sleep apnea syndrome: a review of 35 patients. J Oral Maxillofac Surg 57:382-5

38. Hsu PP, Brett RH (2001) Multiple level pharyngeal surgery for obstructive sleep apnoea. Singapore Med J 42(4):160-4

39. Hendler BH, Costello BJ, Silverstein K, Yen D, Goldberg A (2001) A protocol for uvulopharyngoplasty, mortised genioplasty, and maxillomandibular advancement in patients with obstructive sleep apnea: an analysis of 40 cases. J Oral Maxillofac Surg 59:892

40. Neruntarat C (2003) Genioglossus advancement and hyoid myotomy: short-term and long-term results. J Laryngol Otol 117(6):482-6

41. Verse T, Baisch A, Hormann K (2004) Multi-level surgery for obstructive sleep apnea. Preliminary objective results. Laryngorhinootologie 83(8):516-22

42. Miller FR, Watson D, Boseley M (2004) The role of the Genial bone advancement trephine system in conjunction with uvulopalatopharyngoplasty in the multilevel management of obstructive sleep apnea. Otolarygol Head Neck Surg 130(1):73-9

43. Datillo DJ, Drooger SA (2004) Outcome assessment of patients undergoing maxillofacial procedures for the treatment of sleep apnea: comparison of subjective and objective results. J Oral Maxillofac Surg 62:164-8

44. Hörmann K, Maurer JT, Baisch A (2004) Schnarchen/Schlafapnoe - chirurgisch heilbar? HNO 52:807-12

45. Oksenberg A, Silverberg DS, Arons E, Radwan H (1997) Positional vs nonpositional obstructive sleep apnea patients. Chest 112:629-39

46. Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N. (2006) The role of sleep position in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 263(10):946-50

47. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J (2000) Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 284:301521

48. Hochban W, Brandenburg U, Peter JH (1994) Surgical treatment of obstructive sleep apnea by maxillomandibular advancement. Sleep 17(7):624-9

49. Prinsell JR (1999) Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. Chest 116:1519-29

chapter 6

COMPLICATIONS OF HYOID SUSPENSION IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Abstract

The objectives of the study are to assess adverse events and complications of hyoid suspension (HS) as a treatment of obstructive sleep apnea syndrome (OSAS). The study design was cohort. Thirty-nine patients with OSAS and obstruction at tongue base level, as assessed by sleep endoscopy, underwent HS. Information about adverse events and complications were obtained by reviewing charts and patient-completed questionnaires. The mean follow up period from surgery to last control visit was 13.1 months (range 2-38). The charts demonstrated mainly adverse events. Minor complications occurred in six patients. No major complications were observed. The mean admission duration was 3.3 days (range 2-5). Twenty-six patients (67%) returned their questionnaires. No association was found between completing questionnaires and the success of the intervention (p=0.73). The questionnaires were completed on average 25.9 months (range 3.5-51.5) after surgery. VAS scores showed a fast decline in complaints regarding taste, speech, swallowing and pain. No significant long-term differences were found, when comparing the postoperative VAS scores with the preoperative VAS scores. Of the 26 evaluable questionnaires, 20 patients (77%) would recommend HS to an acquaintance if they suffered from sleep apnea syndrome, when only taking side effects in consideration. The intention to give a positive recommendation did not seem to be related to the therapeutic success of the intervention. In conclusion, this study demonstrates that the complication rate of HS is low and that the discomfort is very acceptable.

Key words. Obstructive sleep apnea syndrome – Hyoid suspension - Complications

Introduction

Obstructive sleep apnea syndrome (OSAS) is recognized as a disease with serious consequences. Besides a negative effect on quality of life, such as severe snoring, daytime sleepiness and decreased intellectual performance,[1, 2] OSAS is associated with increased risks of hypertension, myocardial infarction, stroke and traffic accidents.[3-8] The prevalence is estimated to be between 2% and 4% in middle-aged people.[9]

OSAS is caused by an imbalance between the anatomy of the upper airway and the physiological loss of muscle tone during sleep, resulting in total breathing cessation (apneas) and/or airflow reduction (hypopneas).

During the past decades a variety of treatment modalities have been developed based on the different elements of pathophysiology. These treatment methods can be classified as non-surgical or surgical therapies. Non-surgical therapies include lifestyle alterations such as weight reduction and abstinence of alcohol, sedatives and sleep medication, nasal continuous positive airway pressure (NCPAP) and mandibular repositioning appliances (MRA).[10-13] Surgical treatments are performed based on the level of obstruction in the upper airway and vary from radiofrequency induced thermotherapy (RFTT) of the palate or tongue base, a minimally invasive intervention [14-16] to uvulopalatopharyngoplasty (UPPP),[17] hyoid suspension (HS),[18] genioglossus advancement (GA),[19] maxillomandibular advancement (MMA)[20-22] or tracheostomy[23]. Different surgical interventions can be performed in unilevel (palatal or retrolingual level only) or multilevel (both these levels) procedures, either staged, or simultaneously. Surgical therapies are indicated to treat anatomical abnormalities and when NCPAP is refused or not tolerated.

HS is indicated in patients with moderate to severe OSAS, with a retrolingual obstruction, to avoid more radical surgery, such as maxillomandibular advancement or tracheostomy. This procedure, first described by Riley et al. in 1986, aims at advancement of the hyoid bone and subsequent increase in the retrolingual space.[24] In 1994, the intervention was modified by fixing the hyoid bone to the thyroid cartilage, instead of fixing it upward to the chin.[18] This modern approach was named HS type II or hyoidthyroidpexia. Although hyoidthyroidpexia is the better term, the simpler “Hyoid Suspension” in particular in the US, is more often used. In this paper we will use the term HS referring to HS type II or hyoidthyroidpexia. Previous reports stated that HS was successful in 52-53.3% of patients.[18, 25]. With this paper, we report and evaluate adverse events and complications of HS.

Patients and methods

All patients visiting our department between March 2000 and April 2006 with complaints of habitual snoring and/or suspicion of OSAS were evaluated by history, physical examination, full overnight polysomnography and midazolam or propofol-induced sleep endoscopy.

Polysomnography

Apneas were defined as cessation of oronasal airflow for at least 10 s. Hypopneas were defined as periods of reduction of >30% oronasal airflow during minimally 10 s. The AHI is the mean number of apneas and hypopneas per hour of sleep and defines the severity of OSAS. Mild OSAS is AHI ≥5 and < 15, moderate OSAS is AHI ≥ 15 and < 30 and severe OSAS is AHI ≥ 30.[26]

Patients

Patients with moderate to severe OSAS, retrolingual narrowing or collapse and refusal or non-acceptance of NCPAP treatment were advised HS with or without radiofrequent ablation of the tongue base (RFTB) in one operative session. The decision to add RFTB to the surgery was based on our standard treatment at the time.

Procedure hyoid suspension

After exposure via an external horizontal incision at the level of the thyrohyoid membrane, the strap muscles (sternohyoid muscle, omohyoid muscle and thyrohyoid muscle) were divided just below the hyoid and superior to the hyoid the tendon of the stylohyoid muscle was divided from the hyoid bone. Mobilising the hyoid bone in anterocaudal direction and fixing it permanently to the thyroid cartilage created more space retrolingually.[18]

Per- and postoperative care

Conscientious monitoring of oxygen saturation at the Intensive Care Unit for one night after surgery was regarded mandatory because of the risk of a compromised airway due to postoperative bleeding or oedema. Only in case RFTB was performed simultaneously, patients received 2.5 grams of amoxicillin with clavulanic acid i.v. during surgery and 3 dd 625 mg orally during one week postoperatively; otherwise, no antibiotics were applied. The drain placed during surgery was usually removed within 48 to 72 hours postoperatively depending on the drain production. Oral painkillers were prescribed only when necessary. Steroids were not used routinely.

Adverse events and complications

All patients received questionnaires which included visual analogue scales (VAS) (a scale from 0, normal, to 10, abnormal) for taste, speech and swallowing prior to surgery and taste, speech, swallowing and pain 1 day, 1 week and at time of answering the questionnaire. Lastly, patients were asked whether they would advise HS to an acquaintance if they suffered from OSAS, only taking the side effects and discomfort into account and not the grade of success.

Information about complications was also obtained by reviewing the charts. We divided complications in A) adverse events (spontaneous recovery), B) minor complications (intervention needed, but without residual problems), C) major complications (persistent problems) and D) death.[27]

Statistics

Patient characteristics and results from the completed questionnaires were presented by means and standard deviation. Differences in parameters between different time points were compared using the Wilcoxon signed rank sum test. Because of the explorative character, no adjustments were applied for type I error inflation.

Results

Thirty-nine patients underwent HS. Patient characteristics are shown in table 1. In eight cases, HS was combined with RFTB as part of the standard treatment at the time.

Table 1 Baseline characteristics

Measurement	**HS** ***(n=39)***
Age, year	49.0 ± 10.5
BMI, kg/m^2	27.3 ± 3.2
AHI	30.4 ± 10.1
female : male	5 (13%) : 34 (87%)
RFTB- : RFTB+	31 (79%) : 8 (21%)

BMI: body mass index; AHI: apnea hypopnea index.

The mean follow-up period from surgery to last control visit was 13.1 months (range 2-38). The charts demonstrated mainly adverse events like temporary complaints of pain, swallowing difficulties and increased saliva production. One patient had a deviated tongue for a short period which resolved within a few weeks postoperatively. This patient did not receive

RFTB. Minor complications occurred in six patients. We observed infections in two subjects, a wound abscess in one and fistula in two cases. The patients having infections or wound abscess did not receive RFTB and therefore did not receive prophylactic antibiotics. One patient underwent a tracheotomy within a few hours after surgery, because of an imminent compromised airway due to postoperative bleeding. After 2 days, the tracheotomy was closed again. No major complications were seen. The mean admission duration was 3.3 days (range 2-5 days).

In total, 26 patients (67%) returned their questionnaires of which 23 (59%) were fully evaluable. No association was found between completing questionnaires and the success of the intervention (p=0.73). The questionnaires were completed on average 25.9 months (range 3.5-51.5) after surgery.

Table 2 VAS scores over time

VAS *(n=24)*		Mean
Taste	1 day	2.7±2.6
	1 week	1.2±1.5
	Long term	0.9±1.8
Speech	1 day	2.9±2.7
	1 week	2.3±2.8
	Long term	0.6±0.5
Swallowing	1 day	4.7±3.0
	1 week	2.8±2.9
	Long term	1.1±1.9
Wound pain	1 day	4.1±2.7
	1 week	2.3±2.6
	Long term	0.8±1.2

Table 2 shows the overall VAS scores over time. A fast decline was observed concerning complaints of taste, speech, swallowing and pain. No significant long-term differences were found when comparing the postoperative VAS scores with the preoperative VAS scores (table 3). We did not compare pain with preoperative VAS scores. One patient still reported serious wound pain after 2.5 years with a VAS score of 6.3.

Table 3 VAS scores postoperative compared with preoperative

VAS	1 day	1 week	Long term
Taste	2.1±2.5*	0.6±1.5	0.3±1.9
Speech	2.3±2.8*	1.6±2.9**	0.0±0.8
Swallowing	3.8±3.2*	1.9±2.9*	0.2±2.1

** p < 0.0001*

*** p < 0.01*

Of the 26 questionnaires, 20 patients (77%) would recommend HS to an acquaintance if they suffered from sleep apnea syndrome, when only taking side effects into consideration. The intention to give a positive recommendation did not seem to be related to the therapeutic success of the intervention.

Discussion

OSAS due to obstruction on tongue base level in general can be treated with NCPAP, MRA and surgery. In case NCPAP or MRA therapy is not possible or refused by the patient, surgery is indicated. As previously mentioned, there are several forms of surgery for the tongue base. Established surgical procedures for tongue base obstruction include RFTB, HS, GA and MMA. Although RFTB has very low adverse events and complication rates, the effect is minimal and therefore only indicated exclusively for patients with snoring or mild OSAS or as part of a combined approach.[16] There is no data on the effectiveness of GA as an independent treatment modality. The known risks of GA are long lasting numbness of the lower central incisors, exposure of plates and screws and floor of mouth hematomas.[28] MMA is probably the most successful operation for OSAS, but its morbidity is considerable. Patients need temporary intermaxillary fixation. Furthermore, complications, such as lower lip, chin and cheek anesthesia, temporomandibular joint dysfunction, velopharyngeal insufficiency, and occlusion disturbances are reported.[29,30] Several experimental tongue base procedures are still being investigated, but none are presently at the point that general application can already be advised.

We have published earlier reports on the results of HS [25] and on the results and complications of RFTB [16]. Results of combined HS and RF of the tongue base will be reported in the near future. In the present study, we focused on complications and patient acceptance of HS with/without RFTB. Patients undergoing palatal intervention simultaneously (multilevel surgery) were excluded in this study.

The present study demonstrates that the complication rate of HS is low and its discomforts are acceptable. HS, when taking into consideration both success rates, risks and discomforts, compares favourably with other tongue base surgical procedures. HS, which is performed via an external incision in the neck, seems, at first sight, to be more extensive surgery than for instance UPPP, applied when treating obstruction at palatal level. In reality, however, HS seems to be much less painful as compared to UPPP [31]. Because of the absence of internal mucosal wounds, taste, speech and swallowing are hardly affected. The external scar in the neck is, in the long run, often barely visible, because it is placed in a natural skin line.

In summary, HS should be considered a potential treatment option for moderate to severe OSAS with obstruction at tongue base level. There is a lot of 'work in progress' concerning tongue base treatment options. New procedures, in the future, may prove superior to HS in terms of results and complication rates. Until then, we regard HS as the cornerstone of surgery for tongue base obstruction.

References

1. Chung KF (2000) Use of Epworth's sleepiness scale in Chinese patients with OSA and normal employees. J Psychosom Res 49:367-72
2. Chesire K, Engleman H, Deary I, Shapiro C, Douglas NJ (1992) Factors impairing daytime performance in patients with sleep apnea/hypopnea syndrome. Arch Intern Med 152(3):538-41
3. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342:1378-84
4. Shamsuzzaman ASM, Gersh BJ, Somers VK (2003) Obstructive sleep apnea, implications for cardiac and vascular disease. JAMA 290(14):1906-14
5. Caples SM, Garcia-Touchard A, Somers VK (2007) Sleep-disordered breathing and cardiovascular risk. Sleep 30(3):291-303
6. Dyken ME, Somers VK, Yamada T, Ren ZY, Zimmerman MB (1996) Investigating the relationship between stroke and obstructive sleep apnea. Stroke 27:401-7
7. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J (1999) The association between sleep apnea and the risk of traffic accidents. N Engl J Med 340(11):847-51
8. George CF, Smiley A (1999) Sleep apnea and automobile crashes. Sleep 22(6):790-5
9. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep disordered breathing among middle-aged adults. N Engl J Med 328(17):1230-5
10. Sullivan CE, Issa FG, Berthon-Jones M, Eves L (1981) Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1(8225):862-5
11. (1994) Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Am J Crit Care Med 150:1738-45
12. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18(6):501-10
13. Kushida CA, Morgenthaler TI, Littner MR, Alessi CA, Bailey D, Coleman J Jr, Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Owens J, Pancer JP (2006) Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: an update for 2005. An American academy of sleep medicine report. Sleep 29(2):240-3
14. Powell NB, Riley RW, Troell RJ, Li K, Blumen MB and Guilleminault C (1998) Radiofrequency volumetric tissue reduction of the palate in subjects with sleep-disordered breathing. Chest 113(5):1163-74
15. Stuck BA, Köpke J, Maurer JT, Verse T, Eckert A, Bran G, Duber C, Hormann K (2003) Lesion formation in radiofrequency surgery of the tongue base. Laryngoscope 113:1572-6
16. Den Herder C, Kox D, van Tinteren H, de Vries N (2006) Bipolar radiofrequency induced thermotherapy of the tongue base: its complications, acceptance and effectiveness under local anesthesia. Eur Arch Otorhinolaryngol 263:1031-40
17. Fujita S, Conway W, Zorick F, Roth T (1981) Surgical corrections of anatomical abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 89:923-34
18. Riley RW, Powell NB, Guilleminault C (1994) Obstructive sleep apnea and the hyoid: a revised surgical procedure. Otolaryngol Head Neck Surg 111(6):717-21

19. Kerner MM, Hale RG, Silva Kim (2002) A novel three-piece anterior mandibular visor osteotomyfor genioglossus advancement in surgery for obstructive sleep apnea. Oper Techn Otolaryngol Head Neck Surg 13(2);175-7

20. Hochban W, Brandenburg U, Peter JH (1994) Surgical treatment of obstructive sleep apnea by maxillomandibular advancement. Sleep 17(7):624-9

21. Prinsell JR (1999) Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. Chest 116:1519-29

22. Datillo DJ, Drooger SA (2004) Outcome assessment of patients undergoing maxillofacial procedures for the treatment of sleep apnea: comparison of subjective and objective results. J Oral Maxillofac Surg 62:164-8

23. Simmons FB (1979) Tracheotomy in obstructive sleep apnea patients. Laryngoscope 89:1702-3

24. Riley RW, Powell NB, Guilleminault C (1986) Inferior sagittal osteotomy of the mandible with hyoid myotomy-suspension: a new procedure for obstructive sleep apnea. Otolaryngol Head Neck Surg 94(5):589-93

25. Den Herder C, van Tinteren H, de Vries N (2005) Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. Laryngoscope 115(4):740-5

26. (1999) Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American academy of sleep medicine task force. Sleep 22(5):667-89

27. Rombout J, de Vries N (2001) Complications in sinus surgery and new classification proposal. Am J Rhinol 15(6):363-70

28. Miller FR, Watson D, Boseley M (2004) The role of the genial bone advancement trephine system in conjunction with uvulopalatopharyngoplasty in the multilevel management of obstructive sleep apnea. Otolaryngol Head Neck Surg 130:73-9

29. Li KK, Riley RW, Powell NB, Troell R, Guilleminault C (1999) Overview of phase II surgery for obstructive sleep apnea syndrome. Ear Nose Throat J 78(11): 851, 854-7

30. Li KK, Troell RJ, Riley RW, Powell NB, Koester U, Guilleminault C (2001) Uvulopalatopharyngoplasty, maxillomandibular advancement, and the velopharynx. Laryngoscope 111:1075–8

31. Kokki H, Nikanne E, Aho M, Virtaniemi J (2003) Pain intensity after laseruvulopalatoplasty and tonsillectomy. Otolaryngol Head Neck Surg 128(2):273-9

chapter 7

UPPP COMBINED WITH RADIOFREQUENCY THERMOTHERAPY OF THE TONGUE BASE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Abstract

We investigated the outcome of uvulopalatopharyngoplasty (UPPP) combined with radiofrequency thermotherapy of the tongue base (RFTB) in patients with obstructive sleep apnea syndrome (OSAS) with both palatal and retroglossal obstruction, and we compared these results with the results of single level surgery (UPPP). A retrospective cohort study was performed in patients with mild to severe OSAS who underwent UPPP with or without RFTB. Seventy-five patients with both palatal and retroglossal obstruction underwent UPPP, 38 patients without RFTB (group 1) and 37 patients with RFTB (group 2). The outcome of the surgery was measured by both objective success (defined as a reduction of AHI >50% and AHI below 20) and subjective improvement. In group 1 the overall success rate was 42%, and in group 2 49%. Other polysomnographic values (AI, DI, mean SaO_2) improved after surgery (not significant). No serious adverse events occurred. Surgical treatment of combined palatal and retroglossal obstruction remains a challenge. Adding RFTB to UPPP results in a mild improvement compared to UPPP alone. Although the addition of RFTB to UPPP seems to result in only a limited improvement, there is no major downside to it. RFTB is well-tolerated and safe.

Key words. Obstructive sleep apnea syndrome - Radiofrequency thermotherapy - Tongue base - Uvulopalatopharyngoplasty

Introduction

Uvulopalatopharyngoplasty (UPPP) is still the most frequently used surgical treatment for obstructive sleep apnea syndrome (OSAS). Overall outcomes have been disappointing. Meta-analysis by Sher et al.[1] in 1996 indicated an over-all success rate of only 40.7 %. This meta-analysis showed that the success rates of UPPP are related to the level of obstruction: an objective success rate of 52.3% in patients with only palatal narrowing or collapse, versus 5.3% in patients with a retroglossal obstruction with or without a palatal component.

Improvements in success rates of UPPP are therefore directly related to patient selection and, to a lesser extent, to modifications of UPPP in selected patients. For instance, Friedman et al.[2] have shown that in patients with palatal obstruction, who previously have had a tonsillectomy, it might be better to perform Z-palatoplasty (ZPP). Patients with only retroglossal obstruction should not undergo UPPP at all.

An important category is formed by patients with combined palatal and retroglossal obstruction. Two often-used systems for determination of the level(s) of obstruction are the Modified Mallampati/Friedman system and sleep endoscopy. We have shown previously that our results of UPPP after patients selection with sedated endoscopy are better than average, with success rates of 70-80%, depending on the definition used.[3] Negative predictors of outcome were: combined palatal and retroglossal obstruction and earlier tonsillectomy.[4] In this period we neither used radiofrequency thermotherapy of the tongue base (RFTB), nor hyoid suspension (HS), nor ZPP. Since this report we changed our policy. Post tonsillectomy patients now usually will have Z-palatoplasty. Patients with combined palatal and retroglossal obstruction undergo UPPP (or a modification of it) combined with RFTB with or without HS.[5] In general, in case of mild to moderate OSAS, and palatal and partial retroglossal obstruction as assessed by sedated endoscopy, we combine UPPP and RFTB. Although this approach seems logical, little has been published about results of UPPP with RFTB.

RFTB as only treatment has been proved to be safe, effective, well tolerated and technically simple to perform.[6-9] These advantages make RFTB preferable to use in a multilevel approach together with UPPP, rather than more invasive procedures with a greater risk of complications and morbidity, such as mandibular osteotomy with genioglossus advancement, partial midline tongue resection and hyoid suspension. These operative techniques are preferred in more outspoken, total or subtotal, retroglossal obstruction. Therefore only in case of moderate to severe OSAS, palatal obstruction and total retroglossal obstruction as

assessed by sedated endoscopy, we presently combine UPPP, HS and RFTB, the so called multilevel surgery.[10]

In this study we investigate the value of radiofrequency thermotherapy of the tongue base (RFTB) added to uvulopalatopharyngoplasty (UPPP) in patients with both palatal and retroglossal obstruction. Secondly, we investigate whether this combination of UPPP and RFTB is safe and well-tolerated.

Patients and methods

Patients

We performed a retrospective cohort study. All patients with mild to severe OSAS with both palatal and retroglossal obstruction, who underwent UPPP with or without RFTB in the period from November 2003 until October 2006 in our clinic, were included. Exclusion criteria were an apnea/hypopnea index (AHI) under 5 or over 50 and a medical history with previous UPPP or RFTB or radiofrequency thermotherapy of the palate.

The study population was divided in two groups. In both the groups all the patients had obstruction at palatal and retroglossal level. Group 1 consisted of patients who underwent UPPP alone. Group 2 consisted of patients undergoing multilevel surgery, UPPP combined with RFTB.

Polysomnography

All the patients underwent a preoperative all-night attended comprehensive sleep study using a digital Embla recorder (Flaga Medical devices, Reykjavik, Iceland). Polysomnography (PSG) consisted of electroencephalogram, submental electromyogram and electrooculogram to record the sleep pattern. Pulse oximetry was used to monitor oxygen saturation (SaO_2) and heart rate. Thoracic and abdominal efforts were registered as well as movements of the limbs. Furthermore nasal airflow and snoring were measured by a pressure sensor.

Obstructive apneas were defined as cessation of airflow for at least 10 s. Hypopneas were defined as periods of reduction of >30% oronasal airflow for at least 10 s. The apnea/hypopnea index (AHI) was calculated as the sum of total events (apneas and hypopneas) per hour of sleep; mild OSAS defined as an AHI ≥5, <15, moderate OSAS as an AHI ≥15, <30, and severe OSAS as an AHI ≥30. The desaturation index (DI) was defined as the mean number of desaturations of >4% per hour.

Sleep endoscopy

Sleep endoscopy during sedation with midazolam or propofol was performed in all patients to identify the level(s) of obstruction. Patients were assumed having single level obstruction at palatal or retroglossal level, or having obstruction at both palatal and retroglossal level. Obstruction at retroglossal level was divided in partial and complete obstruction.

Surgical techniques

Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty (UPPP) was carried out according to Fujita's technique. The anterior and posterior tonsillar pillars were trimmed and reoriented and the uvula was excised.[11] A tonsillectomy was performed if tonsils were present (in 64 of 75 patients (85 %)).

Radiofrequency Thermotherapy of the Tongue Base

In the patients in group 2, UPPP was followed by (bipolar) radiofrequency ablation of the tongue base (Celon®) to accomplish stiffening and volume reduction of the tongue base. Energy was delivered with an exclusive needle device through the dorsal surface of the tongue on six sites; each site was treated with a power setting of 7 Watt, which equals ± 42 J (total ± 252 J). All the patients received postoperative antibiotics. Two patients received additional RFTB under local anaesthesia as secondary procedure.

Postoperative evaluation

Surgical success rate was defined as more than 50% reduction of the AHI and AHI below 20. Response rate was defined as reduction of AHI between 20% and 50%.

When a postoperative PSG was not performed, success and response were based on patient's (and/or partner's) opinion regarding the subjective changes of symptoms after treatment. Subjective success was defined as disappearance of snoring and daytime hypersomnolence and response as decrease of snoring and daytime hypersomnolence. It is clinical reality that diagnostic tests, like postoperative PSG, are not performed when treatment seems satisfactory for patient, doctor or both.

Adverse events

Incidents which might have had a negative effect on the surgical outcome were registered. These incidents were classified into four grades of severity. Grade I was an adverse event that resolved if left untreated or required a simple bedside procedure. Grade II was a minor complication that required an additional intervention that involved a risk of its own, but was

eventually resolved. Grade III was a major complication that was associated with a residual or a lasting disability. Grade IV was any complication that resulted in death.[12]

Statistical analysis

T test, Fisher's exact test, and chi-square test were employed to evaluate differences between the two patient groups. The *t* test was used to compare preoperative with postoperative mean values. The Cochran-Armitage Trend test was used to compare success rates.

Results

Baseline

The charts of 75 patients with multilevel obstruction, an AHI ≥5 and < 50 and no previous OSAS surgery were studied retrospectively. Thirty-eight patients were treated with UPPP (group 1) and 37 patients were treated with UPPP and RFTB (group 2). Patient characteristics are shown in Table 1, including age, gender, body mass index (BMI), AHI, AI, DI, mean SaO_2, and whether or not a tonsillectomy was performed. There were no significant differences between the two treatment groups.

Table 1 Baseline

	Palatal and retroglossal obstruction treated with UPPP Group 1, *N*= 38 (51%)		**Palatal and retroglossal obstruction treated with UPPP and RFTB Group 2, *N*=37 (49%)**	
Age	45	(25-67)	49	(29-72)
Gender (male)	35	(92%)	30	(81%)
BMI	26.7	(20.9-32.3)	26.4	(21.8-39.0)
AHI	18.9	(5.4-47)	17.8	(5-42.6)
AI	6.8	(0.3-23)	7.8	(0-36.7)
DI	6.4	(0-20.2)	7.7	(0-41)
Mean SaO_2	95.8	(92-98)	95.3	(91-97.3)
Tonsillectomy	35	(92%)	29	(78%)

Mean patient characteristics of 38 patients with palatal and retroglossal obstruction treated with UPPP and 37 patients with palatal and retroglossal obstruction treated with UPPP and RFTB

Efficacy

Success and response rates are shown in Tables 2 and 3. The group treated with only UPPP (group 1) had an overall success rate of 42%, this rate increased to 49% in the group treated with both UPPP and RFTB (group 2). This difference was not significant (*P*=0.88, Table 2). The success and response rates for the patients treated with UPPP with a tonsillectomy were slightly better than the success and response rates for patients treated with UPPP without tonsillectomy, but not significant (Table 3).

Table 2 Success and response rates

		Palatal and retroglossal obstruction treated with UPPP Group 1, *N*=38 (51%)		**Palatal and retroglossal obstruction treated with UPPP and RFTB Group 2, *N*=37 (49%)**	
Success	**Overall**	16	(42%)	18	(49%)
	Objective	13	(34%)	14	(38%)
	Subjective	3	(8%)	4	(11%)
Response	**Overall**	11	(29%)	7	(19%)
	Objective	9	(24%)	6	(16%)
	Subjective	2	(5%)	1	(3%)

Comparison of overall, objective and subjective success and response rates in patients with palatal and retroglossal obstruction treated with either UPPP or UPPP and RFTB

Table 3 Success and response rates with or without tonsillectomy

	Palatal and retroglossal obstruction treated with UPPP Group 1, *N*=38 (51%)				**Palatal and retroglossal obstruction treated with UPPP and RFTB Group 2, *N*=37 (49%)**			
	With tonsillectomy *N*=35 (92%)		**Without tonsillectomy *N*=3 (8%)**		**With tonsillectomy *N*=29 (78%)**		**Without tonsillectomy *N*=8 (22%)**	
Overall Success	15	(43%)	1	(33%)	15	(52%)	3	(38%)
Overall Response	11	(31%)	-		4	(14%)	3	(38%)

Comparison of overall success and response rate in patients with palatal and retroglossal obstruction treated with either UPPP or UPPP and RFTB, with or without tonsillectomy

Pre- and post-operative values are presented in Table 4. All the polysomnographic variables improved after surgery, although not significant. None of the baseline characteristics could be correlated with predicting the postoperative results.

Table 4 pre- and postoperative values

		Palatal and retroglossal obstruction treated with UPPP Group 1, *N*=38 (51%)	Palatal and retroglossal obstruction treated with UPPP and RFTB Group 2, *N*=37 (49%)
BMI	**Pre**	26.7 ±2.6	26.4 ±3.2
	Post	27.0 ±2.8	25.6 ±2.1
AHI	**Pre**	18.9 ±9.6	17.8 ±10.3
	Post	12.0 ±9.0	11.2 ±10.8
AI	**Pre**	6.8 ±5.4	7.8 ±8.8
	Post	3.9 ±4.5	4.9 ±7.5
DI	**Pre**	6.4 ±5.5	7.6 ±8.9
	Post	3.0 ±3.0	4.3 ±5.9
Mean SaO_2	**Pre**	95.8 ±1.4	95.3 ±1.4
	Post	96.0 ± 1.1	95.7 ±1.3

Comparison of pre- and postoperative polysomnographic data in 75 patients with palatal and retroglossal obstruction treated with either UPPP or UPPP and RFTB

Adverse events

Only a few adverse events occurred. Most were mild and resolved spontaneously or with a simple treatment, grade I/II. After RFTB two patients experienced transient tongue deviation and loss of sensibility, one patient developed a fair amount of edema of the tongue, all resolving without treatment. No major complications, grade II/III, like tongue base abscess, paresis or paralysis, or airway obstruction, occurred.

No major complications, secondary to UPPP, were reported. Four patients had a postoperative haemorrhage, necessitating cauterization (grade II). Temporary postoperative palatal insufficiency was reported in 7 patients and resolved spontaneously in time.

Additional RFTB

In only two patients an extra treatment of the tongue base with radiofrequency thermotherapy followed the initial treatment of UPPP with RFTB. These two patients were both responders.

Discussion

This study shows that adding RFTB to UPPP as treatment for patients with both palatal as retroglossal obstruction leads to a slight, but not significant, improvement in outcome. Adding RFTB to UPPP gave an increase in objective success rate of 17.2%, from 37.9 to 55.1% for Friedman satge II patients and an increase of 24.9%, from 8.1 to 33% for stage III patients. Based on our experience, we expected that adding RFTB to UPPP would give a small but notable improvement. Nelson found an objective success rate of 50% in his patient group (*N*=13) with combined palatal and retroglossal obstruction treated with both UPPP and RFTB. He compared these patients with patients with single level palatal obstruction treated with UPPP; their success rate was 57%. Unfortunately in these small series, a group with multilevel obstruction but single level treatment was not studied.[13]

The value of adding RFTB to UPPP in patients with multilevel obstruction was also confirmed by others.[14-16] Friedman et al.[14] staged their patients with the Friedman staging system. Adding RFTB to UPPP gave an increase in objective success rate of 17.2%, from 37.9 to 51.1% for Friedman stage II patients, in whom the uvula but not the tonsils could be visualized during inspection of the oral cavity, and an increase of 24.9%, from 8.1 to 33.0% for stage III patients, in whom the soft palate but not the uvula could be visualized. The subjective success rates were higher; 95.9% for stage II patients and 84.1% for stage III patients. Jacobowitz [16] indicated objective success rates of 61% in Friedman stage II patients, and even 89% in stage III patients. Both studies confirm the additional value of RFTB next to UPPP, but are not completely comparable with our and Nelson's study. Friedman et al.[15] used their staging system, suggesting that patients with Friedman stages II and III had obstruction at retroglossal level. Sleep endoscopy to objectify the presence and degree of retroglossal obstruction was not performed. We prefer an extended diagnostic workup, including Friedman staging, polysomnography and sleep endoscopy to objectify the levels of obstruction.[3] In the study of Jacobowitz the success rates are high, but based on a very small population (*N*=5 for UPPP+RFTB).

In this study, we found that success rates were slightly better in the patient group treated with UPPP including tonsillectomy. For the patients in which this treatment was not followed by RFTB the success rate improved from 33 without tonsillectomy to 43% with tonsillectomy (group 1). For the patients who also underwent RFTB the success rate changed even more from 38 without tonsillectomy to 52% with tonsillectomy (group 2). This confirms our earlier findings and of others about the negative effect of previous tonsillectomy on the results of OSAS surgery.[2,4]

It was already reported in other studies that RFTB is a minimal invasive, safe procedure. [6,8,13,14,16] We also found that RFTB added to UPPP is technically straightforward, easy to perform, safe, and well tolerated. The addition of RFTB to UPPP did not lead to serious adverse events, like tongue base abscess or airway obstruction. Stuck et al.[17] advise 600 J at 85 ºC as optimal energy level leading to optimal lesion size with minimal side effects. In our clinic a total of 252 J is delivered to the tongue base per session. This lower energy level might lead to fewer complications, but will also lead to less volume reduction and thereby minimizing the effect of RFTB. Because we are aware of this, we always advise patients to undergo an additional RFTB-treatment. This study shows that this was only done in a few cases.

Beside this limitation, our study has some other limitations. It is a retrospective cohort study with a small patient group. The slight increase of 42% to 49% success is as expected, but to make this improvement statistically significant, much more patients would be needed.

To receive more information whether or not adding RFTB to UPPP is successful in multilevel obstructed, both palatal as retroglossal, patients with mild to moderate OSAS, more research will be necessary. Ideally this would be a prospective, randomized trial, with larger treatment groups, including an optimal additional treatment of RFTB.

In conclusion, **s**urgical treatment of combined palatal and retroglossal obstruction remains a challenge. Adding RFTB to UPPP, results in mild improvement in patients with mild to severe OSAS. Although its efficacy is low, the approach appears to be well-tolerated and safe.

References

1. Sher AE, Schechtman KB, Piccirillo JF (1996) The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 19:156-77
2. Friedman M, Ibrahim HZ, Vidyasagar R, Pomeranz J, Joseph NJ (2004) Z-palatoplasty (ZPP): a technique for patients without tonsils. Otolaryngol Head Neck Surg 131:89-100
3. Hessel NS, de Vries N (2003) Results of uvulopalatopharyngoplasty after diagnostic workup with polysomnography and sleep endoscopy: a report of 136 snoring patients. Eur Arch Otorhinolaryngol 260:91-5
4. Hessel NS, Vries N (2004) Increase of the apnoea-hypopnoea index after uvulopalatopharyngoplasty: analysis of failure. Clin Otolaryngol Allied Sci 29:682-5
5. den Herder C, van Tinteren H, de Vries N (2005) Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. Laryngoscope 115:740-5
6. den Herder C, Kox D, van Tinteren H, de Vries N (2006) Bipolar radiofrequency induced thermotherapy of the tongue base: Its complications, acceptance and effectiveness under local anesthesia. Eur Arch Otorhinolaryngol 263:1031-40
7. Powell NB, Riley RW, Guilleminault C (2003) Radiofrequency tongue base reduction in sleep-disordered breathing: A pilot study. Otolaryngol Head Neck Surg 120:656-64
8. Riley RW, Powell NB, Li KK, Weaver EM, Guilleminault C (2003) An adjunctive method of radiofrequency volumetric tissue reduction of the tongue for OSAS. Otolaryngol Head Neck Surg 129:37-42
9. Woodson BT, Nelson L, Mickelson S, Huntley T, Sher A (2001) A multi-institutional study of radiofrequency volumetric tissue reduction for OSAS. Otolaryngol Head Neck Surg 125:303-11
10. Richard W, Kox D, den Herder C, van Tinteren H, de Vries N (2007) One stage multilevel surgery (uvulopalatopharyngoplasty, hyoid suspension, radiofrequent ablation of the tongue base with/without genioglossus advancement), in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 264:439-44
11. Fujita S, Conway W, Zorick F, Roth T (1981) Surgical correction of anatomic abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 89:923-34
12. Rombout J, de Vries N (2001) Complications in sinus surgery and new classification proposal. Am J Rhinol 15:363-70
13. Nelson LM (2001) Combined temperature-controlled radiofrequency tongue reduction and UPPP in apnea surgery. Ear Nose Throat J 80:640-4
14. Friedman M, Ibrahim H, Lee G, Joseph NJ (2003) Combined uvulopalatopharyngoplasty and radiofrequency tongue base reduction for treatment of obstructive sleep apnea/hypopnea syndrome. Otolaryngol Head Neck Surg 129:611-21
15. Friedman M, Ibrahim H, Joseph NJ (2004) Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope 114:454-9
16. Jacobowitz O (2006) Palatal and tongue base surgery for surgical treatment of obstructive sleep apnea: a prospective study. Otolaryngol Head Neck Surg 135:258-64
17. Stuck BA, Köpke J, Maurer JT, Verse T, Eckert A, Bran G, Duber C, Hormann K (2003) Lesion formation in radiofrequency surgery of the tongue base. Laryngoscope 113:1572-6

chapter 8

DISCUSSION/FUTURE PERSPECTIVES

Since OSAS was only first reported in the late sixties of the last century, it represents a relatively new disease entity, and it is an area in ENT surgery where many changes and improvements occur, with high velocity, both in diagnostic work-up and therapy.

Over the past six years five academic theses have been written about OSAS in The Netherlands and Belgium. In 2004 Hessel wrote about the importance of sleep registration and the added value of sleep endoscopy in the treatment of OSAS by UPPP. In 2007 Vanderveken wrote about the Forced Oscillation Technique to ascertain the degree of upper airway patency in obstructive and central SAS. He also described the effect of adjuvant postoperative administration of acetazolamide after UPPP. Furthermore he discussed the research into a new thermoplastic MRA and the use of an upper airway model based on a CT-scan to predict the success rate of MRA treatment. Hoekema, too, defended his thesis in 2007 and evaluated the specific role of intraoral devices in OSAS patients. In 2010 Hamans obtained a doctorate with a dissertation on the diagnostics and therapy of OSAS with special attention to the role of drug-induced sleep endoscopy, hyoid expansion as a new procedure for OSAS in patients with hypopharyngeal lateral wall collapse and the treatment of tonguebase obstruction with a two-fold tongue implant (tissue anchor and bone anchor). In 2011 Araab defended her thesis about night-to-night variability and the efficacy of adjustable MRA vs nCPAP.

In 2001 the first guideline on the diagnostics and treatment of OSAS in adults appeared. This guideline was drawn up by the Dutch Institute for Healthcare Improvement (Kwaliteitsinstituut voor de Gezondheidszorg). This institute was founded in 1979 as Central Accompagnement Organization (Centraal Begeleidings Orgaan,CBO) for peer review.[CBO-richtlijn, 2001] In 2009 the revised version of this guideline was published.[CBO-richtlijn, 2009] On examination, the differences between these two guidelines immediately become clear though there were only eight years between them. Where in 2001 the emphasis was mainly on the treatment with nCPAP, the second version devotes a great deal of attention to the surgical possibilities and the accompanying diagnostics necessary for proper patient selection.

This thesis describes the introduction of a few new developments in OSAS in the Netherlands.

In chapter 2 we consider whether improvements in nCPAP technology during the last few years, particularly the introduction of APAP, have led to better acceptance and (long-term) compliance in patients with obstructive sleep apnea syndrome (OSAS). About 59.5% of the OSAS patients with nCPAP prescriptions may be regarded as compliant, meaning that they use nCPAP for a minimum of 4 hours per night for at least 5 days a week. There is no

statistical difference between so-called fixed-pressure nCPAP and APAP. We reached quite a large group of nCPAP users in our clinic. Unfortunately, the study remains a retrospective, non randomized, cohort study. The decision to prescribe either nCPAP or APAP was dependent on the period in which patients went to the outpatient clinic. NCPAP use was estimated by the patient and not recorded by a clock-time counter, and it can therefore not be excluded that the actual use is even lower. In addition, there was a wide follow up range (2 months to 8 years).

The role of sleep position in OSAS is described in chapters 3 and 4. Position therapy to treat patients with position dependent OSAS, which until now has remained undervalued, has been further examined. Positional sleep apnea syndrome, defined as having a supine apnea hypopnea index which is twice as high as the apnea hypopnea index in the other positions or more, occurs in 56% of obstructive sleep apnea patients. In our study the mean AHI dropped from 27.7 (ND) to 12.8 (DON) ($p<0.05$) using a neck worn device which influences sleep position by offering a vibration when in supine position. The results of this randomized controlled single blind trial are very promising. A simple device makes it possible to achieve good results, even without nCPAP or operation. A matter that deserves attention in future research is the position of the position sensor. It was found that the supine AHI varied enormously. The average supine AHI even became significantly lower with DON. Also, comparing ND and DOFF, the supine AHI went down even though the patients spent the same amount of time lying on their backs. An explanation for this might be that it is possible that, if a patient on his back only turns his neck because of the device, the position sensor, attached to the torso, indicates supine position and therefore does not vibrate while the head is turned sideways. The occurence of obstructive sleep apnea depends not solely on the position of the torso but also on the position of the head.[Van Kesteren, 2011] In future research the position sensor should therefore not be placed on the torso but on the forehead.

The surgical outcome of a single-session multilevel surgical approach of the upper airway (UPPP, HS, RFTB with/without GA) to treat patients with moderate to severe OSAS and multilevel obstruction is shown in chapter 5. Surgical results of UPPP combined with RFTB in patients with minor to moderate OSAS and both palatal and retrolingual obstruction compared to the results of only UPPP are shown in chapter 7. These surgical procedures are examples of new therapies. Although the groups are too small to allow definite conclusions and there is no randomized control research, multi-level surgery seems promising. However, adding RFTB to UPPP hardly seems to give any added value. Yet, we have demonstrated again that there were no complications, at least in these groups of patients. With this in mind the decision may be taken to carry out RFTB as a therapy additional to a UPPP. Unfortunately, not

all the results in chapter 7 are based on objective data. It is clinical reality that diagnostic tests, like postoperative PSG, are not performed when treatment seems satisfactory for the patient, the doctor or both. Obviously, this would have been desirable for research purposes. In Chapter 6 we investigate adverse events and complications of HS as a treatment of OSAS with obstruction only on tongue base level. This study demonstrates that the complication rate is low and the discomfort is very acceptable. The reliability of the answers to the questionnaire is not ideal as it concerns a retrospective study and patients often only got the questionnaire long after their operation. Still, it provides a clear idea of whether the patients experienced it as very unpleasant or as quite bearable.

NCPAP works, if acceptable to the patient. Unfortunately, many patients experience nCPAP therapy as obtrusive and the acceptance and (long-term) compliance are at best moderate. [Sanders, 1986;Nino-Murcia, 1989;Waldhorn, 1990;Krieger, 1992;Hoffstein, 1992;Kribbs, 1993;Rauscher, 1993;Meurice, 1994;Pieters, 1996;Lojander, 1996;Pepin, 1999;Popescu, 2001;Hui, 2001;Sin, 2002] It is easy to see why this is the reason that so much effort is put into new treatment strategies. In order to make the chance of success for these treatment strategies as big as possible, it is necessary to review the diagnostics accordingly.

Apart from using polysomnography to diagnose OSAS and determine its severity and any position dependence, the level of obstruction in the upper airway has to be researched further as well. Although the ultimate diagnostic method for this has not been found yet, it is logical to assume that a combination of the Friedman staging system [Friedman, 2002;Friedman, 2004] and sleep endoscopy plays an important part. The research into the level of obstruction with the aid of these diagnostic means helps to determine which treatment options are the best for a particular patient.

Furthermore, it must not be forgotten that it is not only the physician's but also the patient's responsibility to assess the actual severity of the problem. A number of questions have to be answered to determine this. Is, apart from the disorder itself, also the complaint serious enough to undergo a certain treatment? It is a known fact that the level of the AHI is poorly correlated to the ESS.(Nguyen, 2006] The severity of the disorder and the severity of the complaints may differ from each other quite a lot because of this. What are the risks involved in treating or refraining from treating the patient? The severer the OSAS, the greater the possible cardiovascular risks.[Veale, 2000; Marti, 2002;Lavie, 2007] What are you prepared to accept for it? A rigorous regime of losing weight if necessary, nCPAP or an enforced sleeping position for the rest of your life, or, possibly, an operation with potential complications? Is treatment

required solely for the OSAS, or does the snoring that frequently accompanies it also drive the patients towards a certain treatment? Is it for yourself or for another? These questions are crucial for a final decision. Obviously, answering these questions is not just a task for the doctor but also for the patient.

It is of great importance for the patient to be aware of all the possibilities during the treatment consultation. Both surgical and non-surgical treatment options have to be discussed. Naturally, these treatment options are to be narrowed down to apply to the patient's situation. When discussing these options special attention must be paid to the severity of the disorder and the level of obstruction as well as the wishes and personal preferences of the patient.

In conclusion, we are witnessing an increasing awareness in the ENT community that we stand at the beginning of an exciting new era in OSAS treatment. NCPAP will not be maintained as first treatment of choice for all patients. In the coming period, a gradual shift can be expected to take place. Alternative treatments will be implemented on well-selected, well-informed, self-responsible patients, with nCPAP therapy still in reserve in case of failure.

Future perspectives

A variety of promising surgical alternatives has recently been and is still being developed by surgical companies and results of those new techniques can be expected in the near future. Also, more emphasis is put on weight reduction programmes for patients who are overweight to obese. In particular for extremely obese OSAS patients, interventions like gastric bypass operations can be considered. In addition, the potential role of positional therapy, which means that the patient has to avoid sleeping in supine position, should be explored further as well.

chapter 9

SUMMARY/SAMENVATTING

9.1 Summary

Chapter 1

This chapter descibes the history, epidemiology, pathophysiology and consequences of obstructive sleep apnea syndrome (OSAS). This is followed by an explanation of the physical examination whose main aim is to draw up a treatment plan and a survey of the various therapeutic options. This chapter concludes with an outline of the thesis.

Chapter 2

Nasal continuous airway pressure (nCPAP) is the most effective conservative treatment of OSAS. The upper airway is kept open by means of air blown into it via the nose. Unfortunately, the use of nCPAP, although effective when used, is not very comfortable. In this chapter we evaluate the actual use (the compliance) of nCPAP when this has been prescribed to patients. On the basis of our results we try, moreover, to determine whether improvements in nCPAP technology have led to better acceptance and (long-term) compliance when compared to data published earlier. We pay special attention to the development of auto-CPAP (APAP) which continuously adapts the required pressure to the patient's needs. About 59.5% of the OSAS patients with nCPAP prescriptions may be regarded as compliant, meaning that they use nCPAP for a minimum of 4 hours per night for at least 5 days a week. There is no statistical difference between so-called fixed-pressure CPAP and APAP. It has become clear that neither the severity of OSAS nor the subjective complaints of the patient influence compliance.

Chapter 3

It is well known that many snorers snore less loud when they turn on their side. In OSAS patients the number of apneas is often reduced when lying on their side. Chapter 3 analyses to what extent sleeping position plays a part in OSAS. Our analysis shows that 55.8% of OSAS patients is position dependent. This implies that when lying on their back, their apnea-hypopnea index (AHI, the avarage number of apneas and hypopneas per hour) is at least twice as high as the average AHI of the other sleeping positions. The body mass index (BMI) and the AHI were higher in the non-position-dependent group, but the difference was not significant in this study. It seemed, moreover, that position-dependent patients had more obstruction at tongue base level than at palatal level. This, too, proved not significant.

Chapter 4

This chapter contains the results of a randomized controlled single blind trial study into the effect of a certain device on sleeping position and therefore also the effect on OSAS in patients

with position-dependent OSAS. This device is attached to the neck and vibrates when the patient turns on his back. In our study the mean AHI dropped from 27.7 (ND) to 12.8 (DON) ($p<0.05$). These results are very promising. A simple device makes it possible to achieve good results, even without nCPAP or operation.

Chapter 5

OSAS patients have an obstruction in the upper airway. This obstruction may be found anywhere from the nose to the larynx. Usually there is a problem at palatal level or tongue base level. Many patients, especially those with severer forms of OSAS, have obstructions at both levels (multilevel obstruction). Patients for whom nCPAP is not an option may be considered for surgery. In order to help these patients as efficiently as possible, operations at both obstruction levels can be performed in one session. This chapter contains the surgical results of this multilevel surgery (uvulopalatopharyngoplastic surgery, hyoid suspension (HS), radiofrequency thermotherapy of the tongue base (RFTB) with/without genioglossus advancement). We have found a significant difference in the average preoperative and postoperative AHI. Including the genioglossus advancement has not appeared to add anything to the success. The success percentage, defined as an AHI<20 and an AHI reduction >50%, was 45%. The response percentage, defined as an AHI reduction of 20-50%, was 27%. So the overall response was 72%. It also became clear that there was no success at all for patients with an AHI of over 55.

Chapter 6

Patients with an obstruction at tongue base level and moderate to severe OSAS, for whom nCPAP, for whatever reason, is not an option, may be considered for HS on its own or as part of multilevel surgery as described in chapter 5. This chapter contains the results of our research into the complications and discomforts after HS performed on its own. Mainly temporary discomforts occurred, patients complained of pain, difficulty when swallowing, and increased saliva production. Six out of 39 patients suffered a minor complication. These patients needed post-operative antibiotics and/or an additional operation. They all recovered completely, although one patient who needed a tracheotomy was left with a scar. This research shows that the risk of complications of HS is low and that the discomfort is acceptable.

Chapter 7

Patients with milder forms of OSAS may also suffer from multilevel obstruction. If sleep endoscopy shows the obstruction to be more prominent at palatal level than at tongue base level, the surgeon may decide to perform UPPP with RFTB, without HS. This chapter contains

the results of our research, comparing UPPP with RFTB and UPPP on its own, for this group of patients. It turned out that adding RFTB to UPPP resulted in a marginally higher success percentage than UPPP alone, but this result was not significant in this study.

Chapter 8
The results described in this thesis are put into a wider context in this chapter.

9.2 Samenvatting

Hoofdstuk 1
In dit hoofdstuk worden de historie, de epidemiologie, de definitie, de pathofysiologie en de consequenties van het obstructief slaap apneusyndroom (OSAS) beschreven. Vervolgens wordt het lichamelijk onderzoek uitgelegd wat speciaal toegespitst is op het vervaardigen van een behandelplan en wordt een overzicht van de verschillende therapeutische opties gegeven. Dit hoofdstuk sluit af met een omschrijving van de doelen van de verschillende onderzoeken van dit proefschrift.

Hoofdstuk 2
Nasal continuous positive airway pressure (nCPAP) is de meest effectieve conservatieve behandeling voor OSAS. Door middel van lucht, die via de neus in de bovenste luchtweg wordt geblazen, wordt de bovenste luchtweg open gehouden. Helaas is het gebruik van nCPAP, hoewel het wanneer het gebruikt wordt effectief is, niet erg comfortabel. In dit hoofdstuk evalueren we het daadwerkelijke gebruik (compliance) van nCPAP wanneer patiënten dit voorgeschreven hebben gekregen. Verder proberen we met onze resultaten aan te geven of verbeteringen in nCPAP technologie geleid hebben tot betere acceptatie en (lange termijn) compliance in vergelijking met eerder gepubliceerde data. Vooral de ontwikkeling van auto-CPAP (APAP), wat de benodigde druk elke keer weer aanpast aan de behoefte van de patiënt, wordt in dit hoofdstuk tegen het licht gehouden. Ongeveer 59,5% van de OSAS patiënten die nCPAP hebben voorgeschreven gekregen kunnen als compliant worden beschouwd. Dit houdt in dat zij minimaal 4 uur/nacht gedurende ≥5 dagen/week nCPAP gebruiken. Er is geen statistisch verschil tussen de zogenaamde fixed pressure CPAP en de APAP. Het blijkt dat de ernst van de OSAS en de subjectieve klachten van de patiënt geen invloed hebben op de compliance.

Hoofdstuk 3
Het is bekend dat veel snurkers minder hard snurken wanneer zij op hun zij slapen. Bij OSAS patiënten is het aantal apneus in zijligging vaak verminderd. In dit hoofdstuk analyseren wij in hoeverre slaappositie een rol speelt bij OSAS. Uit onze analyse blijkt dat 55.8% van de patiënten met OSAS positieafhanlijk zijn. Dat wil zeggen dat zij in rugligging een minstens twee keer zo hoge apneu-hypopneu index (AHI, het gemiddeld aantal ademstops en ademverminderingen per uur), hebben dan de gemiddelde AHI van de andere posities. De body mass index (BMI) en de AHI was hoger in de niet-positieafhankelijke groep, maar dit verschil was in deze studie niet significant. Ook leek het dat positieafhankelijke patiënten meer tongbasis obstructie hadden dan obstructie op palatinaal niveau. Ook dit bleek niet significant.

Hoofdstuk 4
In dit hoofdstuk worden de resultaten gepresenteerd van een gerandomiseerd enkel blind onderzoek naar het effect van een bepaald apparaat op slaappositie en daarmee ook het effect op OSAS bij patiënten met positieafhankelijke OSAS. Dit apparaat wordt op de nek bevestigd en geeft een trilling op het moment dat de patiënt op de rug gaat liggen. In onze studie daalt de AHI van 27.7 (ND) naar 12.8 (DON) ($p<0.05$). Deze resultaten zijn veelbelovend. Met dit simpele apparaat kunnen goede resultaten verkregen worden zonder nCPAP of operatie.

Hoofdstuk 5
Patiënten met OSAS hebben een obstructie in de bovenste luchtweg. Deze obstructie kan zich bevinden vanaf de neus tot aan het strottenhoofd. Meestal gaat het om een probleem op verhemelte- en/of tongbasis niveau. Veel patiënten, met name patiënten met ernstiger vormen van OSAS, hebben obstructie op beide niveaus (multilevel obstructie). Patiënten voor wie nCPAP geen optie is kunnen in aanmerking komen voor chirurgie. Om deze patiënten zo efficiënt mogelijk te helpen kan een operatie op beide obstructie niveaus verricht worden in één ingreep. In dit hoofdstuk rapporteren we onze chirurgische resultaten van deze multilevel chirurgie (uvulopalatopharyngoplastiek, hyoidsuspensie (HS), radiofrequente thermotherapy van de tongbasis (RFTB) met/zonder genioglossus advancement). Er werd een significant verschil gezien in de gemiddelde preoperatieve en postoperatieve AHI. Het toevoegen van de genioglossus advancement leek niet van toegevoegde waarde. Het succespercentage, gedefinieerd als een AHI<20 en >50% reductie van de AHI, was 45%. Het response percentage, gedefinieerd als een AHI reductie van 20-50%, werd gezien in 27% van de gevallen. De overall response was dus 72%. Verder bleek dat bij de patiënten met een AHI boven de 55 geen success werd verkregen.

Hoofdstuk 6

Patiënten met obstructie op tongbasis-niveau met matig tot ernstig OSAS, voor wie nCPAP om wat voor reden dan ook geen optie is, komen in aanmerking voor HS als enige therapie of als onderdeel van multilevel chirurgie zoals beschreven in hoofdstuk 5. In dit hoofdstuk laten we de resultaten zien van ons onderzoek naar complicaties en ongemakken na HS als enige behandeling. Met name tijdelijke ongemakken, zoals klachten van pijn, moeilijkheden bij het slikken en toegenomen speeksel productie, kwamen voor. Zes van de 39 patiënten kregen een complicatie die niet spontaan over ging. Deze patiënten hadden postoperatief antibiotica en/of een extra ingreep nodig. Zij zijn restloos genezen, hoewel één patiënt die een tracheotomie nodig had resteerde met een litteken. Deze studie heeft laten zien dat her risico op complicaties van HS erg laag zijn en dat het ongemak acceptabel is.

Hoofdstuk 7

Patiënten met lichte vormen van OSAS kunnen ook multilevel obstructie hebben. Indien bij slaapendoscopie de obstructie op palatinaal niveau meer op de voorgrond staat dan op tongbasis niveau kan besloten worden tot het verrichten van een UPPP met RFTB, zonder HS. In dit hoofdstuk beschrijven we de resultaten van UPPP gecombineerd met RFTB, vergeleken met UPPP alleen, bij deze groep patiënten. Het bleek dat het toevoegen van RFTB aan UPPP een marginaal hoger succespercentage geeft dan UPPP alleen. Dit resultaat was in deze studie niet significant.

Hoofdstuk 8

De resultaten die in dit proefschrift staan beschreven worden in dit hoofdstuk in een bredere context geplaatst.

APPENDICES

Abbreviations

AHI: apnea hypopnea index
APAP: automatic positive airway pressure
BIPAP: bilevel positive airway pressure
DOFF: device attached in OFF modus
DON: device attached in ON modus
ECG: electrocardiogram
EEG: electroencephalogram
ESS: Epworth sleepiness scale
GA: genioglossus advancement
HS: hyoid suspension
MMA: maxillomandibular advancement
MRA: mandibular repositioning appliance
MSLT: multiple sleep latency test
MWT: maintenance of wakefulness test
NCPAP: nasal continuous positive airway pressure
ND: no device
NO: nitric oxide
NREM: non rapid eye movement
OSAS: obstructive sleep apnea syndrome
PMLS: periodic limb movement syndrome
POSAS: position dependent OSAS
PDG: polysomnography
RAUP: radiofrequency-assisted uvulopalatoplasty
REM: rapid eye movement
RERA: respiratory effort related arousal
RFTB: radiofrequent ablation of the tongue base
SaO_2: oxygen saturation
UPPP: uvulopalatopharyngoplasty
VAS: Visual Analogue Scale
ZPP: Z-palatoplasty

References

- AASM. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American academy of sleep medicine task force. Sleep 1999;22(5):667-89

- Ayas NT, Patel SR, Malhotra A, Schulzer M, Malhotra M, Jung D, Fleetham J, White DP. Auto-titrating versus standard continuous positive airway pressure for the treatment of obstructive sleep apnea: results of a meta-analysis. Sleep 2004;27(2):249-53

- Baguet JP, Hammer L, Lévy P, Pierre H, Rossini E, Mouret S, Ormezzano O, Mallion JM, Pépin JL. Night-time and diastolic hypertension are common and underestimated conditions in newly diagnosed apnoeic patients. J Hypertens 2005;23(3):521-7

- Bassiouny A, El Salamawy A, Abd El-Tawab M, Atef A. Bipolar radiofrequency treatment for snoring with mild to moderate sleep apnea: a comparative study between the radiofrequency assisted uvulopalatoplasty technique and the channeling technique. **Eur Arch Otorhinolaryngol** 2007;264(6):659-67

- Berry S, Roblin G, Williams A, Watkins A, Whittet H. Validity of sleep nasendoscopy in the investigation of sleep related breathing disorders. Laryngoscope 2005;115:538-40

- Burwell CS, Robin ED, Whaley RD, Bickelmann AG. Extreme obesity associated with alveolar hypoventilation-A Pickwickian Syndrome. Am J Med 1956;21(5):811-8

- Buyse B. Sleep apnoea, hypertension and vascular disease: where are we now? Eur Respir Rev 2007;16:169-82

- Buyse B. Treatment effects of sleep apnoea: where are we now? Eur Respir Rev 2007;16: 146-68

- Camilleri AE, Ramamrthy L, Jones PH. Sleep endoscopy: what benefit to the man-agement of snorers? J Laryngol Otol 1995;109:1163-5

- Caples SM, Garcia-Touchard A, Somers VK. Sleep-disordered breathing and cardiovascular risk. Sleep 2007;30(3):291-303

- Cassisi NJ, Biller HF, Ogura JH. Changes in arterial oxygen tension and pulmonary mechanics with the use of posterior packing in epistaxis: a preliminary report. Laryngoscope 1971;81(8):1261-6

- Connor J, Whitlock G, Norton R, Jackson R. The role of driver sleepiness in car crashes: a systematic review of epidemiological studies. Accid Anal Prev 2001;33(1):31-41

- Dickens C. The Posthumous Papers of the Pickwick Club 1837

- Friedman M, Ibrahim H, Bass L. Clinical staging for sleep-disordered breathing. Otolaryngol Head Neck Surg 2002;127(1):13-21

- Friedman M, Ibrahim H, Joseph NJ. Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope 2004;114(3):454-9

- Friedman M, Tanyeri H, Lim JW, Landsberg R, Vaidyanathan K, Caldarelli D. Effect of improved nasal breathing on obstructive sleep apnea. Otolaryngol Head Neck Surg 2000;122(1):71-4

- Friedman M, Ibrahim HZ, Vidyasagar R, Pomeranz J, Joseph NJ. Z-palatoplasty (ZPP): a technique for patients without tonsils. Otolaryngol Head Neck Surg 2004;131(1):89-100

- Fujita S, Conway W, Zorick F, Roth T. Surgical corrections of anatomical abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 1981;89:923–34

- Gastaut H, Tassinari CA, Duron B. Polygraphic study of diurnal and nocturnal (hypnic and respiratory) episodal manifestations of Pickwick syndrome. Rev Neurol (Paris) 1965;112(6):568-79

- Gay P, Weaver T, Loube D, Iber C. Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. Sleep 2006;29:381-401

- Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airway pressure for obstructive sleep apnoea in adults. Cochrane Database Syst Rev 2008;4:CD001106

- Gotsopoulos H, Chen C, Qian J, Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea. A randomized, controlled trial. Am J Respir Crit Care Med 2002;166:743–8

- Guilleminault C, Simmons FB, Motta J, Cummiskey J, Rosekind M, Schroeder JS, Dement WC. Obstructive sleep apnea syndrome and tracheostomy. Long-term follow-up experience. Arch Intern Med 1981;141(8):985-8

- Haines KL, Nelson LG, Gonzalez R, Torrella T, Martin T, Kandil A, Dragotti R, Anderson WM, Gallagher SF, Murr MM. Objective evidence that bariatric surgery improves obesity-related obstructive sleep apnea. Surgery 2007;141(3):354-8

- He J, Kryger MH, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest 1988;94:9-14

- Heitmann J, Ehlenz K, Penzel T, Becker HF, Grote L, Voigt KH, Hermann Peter J, Vogelmeier C. Sympathetic activity is reduced by nCPAP in hypertensive obstructive sleep apnoea patients. Eur Respir J 2004;23:255-62

- Den Herder C, Kox D, van Tinteren H, de Vries N. Bipolar radiofrequency induced thermotherapy of the tongue base: Its complications, acceptance and effectiveness under local anesthesia. Eur Arch Otorhinolaryngol 2006;263(11):1031-40

- Den Herder C, van Tinteren H, de Vries N. Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. Laryngoscope 2005;115(4):740-5

- Hillman DR, Walsh JH, Maddison KJ, Platt PR, Kirkness JP, Noffsinger WJ, Eastwood PR. Evolution of changes in upper airway collapsibility during slow induction of anesthesia with propofol. Anesthesiology 2009;111:63-71

- Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis 1992;145(4 Pt 1):841-5 - Horstmann S, Hess CW, Bassetti C, Gugger M, Mathis J. Sleepiness-related accidents in sleep apnea patients. Sleep 2000;23(3):383-9

- Howard ME, Desai AV, Grunstein RR, Hukins C, Armstrong JG, Joffe D, Swann P, Campbell DA, Pierce RJ. Sleepiness, sleep-disordered breathing, and accident risk factors in commercial vehicle drivers. Am J Respir Crit Care Med 2004;170(9):1014-21

- Hochban W, Conradt R, Brandenburg U, Heitmann J, Peter JH. Surgical maxillofacial treatment of obstructive sleep apnea. Plast Reconstr Surg 1997;99(3):619-26; discussion 627-8

- Hoekema A, Stegenga B, de Bont LGM. Efficacy and co-morbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: a systematic review Crit Rev Oral Biol Med 2004;15: 137-55

- Hörmann K. An update on sleep disordered breathing 2006;chapter 1:11-34

- Hui DS, Choy DK, Li TS, Ko FW, Wong KK, Chan JK, Lai CK. Determinants of continuous positive airway pressure compliance in a group of Chinese patients with obstructive sleep apnea. Chest 2001;120(1):170-6

- Ip MSM, Lam B, Chan LY, Zheng L, Tsang KWT, Fung PCW, Lam WK. Circulating nitric oxide is suppressed in obstructive sleep apnea and is reversed by nasal continuous positive airway pressure. Am J Respir Crit Care Med 2000;162:2166-71

- Iwanaga K, Hasegawa K, Shibata N, Kawakatsu K, Akita Y, Suzuki K, Yagisawa M, Nishimura T. Endoscopic examination of obstructive sleep apnea syndrome patients during drug-induced sleep. Acta Otolaryngol Suppl 2003;(550):36-40

- Johal A, Hector MP, Battagel JM, Kotecha BT. Impact of sleep nasendoscopy on the outcome of mandibular advancement splint therapy in subjects with sleep-related breathing disorders. J. Otolaryngol Otol 2007;121:668-75

- Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1991;149(6):540-5

- Johnston CD, Gleadhill IC, Cinnamond MJ, Gabbey J, Burden DJ. Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. Eur J Orthod 2002;24(3):251-62

- Kerner MM, Hale RG, Silva Kim. A novel three-piece anterior mandibular visor osteotomy for genioglossus advancement in surgery for obstructive sleep apnea. Oper Techn Otolaryngol Head Neck Surg 2002;13(2):175-7

- Kerr P, Millar T, Buckle P, Kryger M. The importance of nasal resistance in obstructive sleep apnea syndrome. J Otolaryngol 1992;21(3):189-95

- Van Kesteren ER, van Maanen JP, Hilgevoord AAJ, Laman DM, de Vries N. Quantitative effects o trunk and head position on the apnea hypopnea index in obstructive sleep apnea. Sleep 2011;34:1075-81

- Kezirian EJ, White DP, Malhotra A, Ma W, McCulloch CE, Goldberg AN. Interrater reliability of drug-induced sleep endoscopy. Arch Otolaryngol Head Neck Surg 2010;136(4):393-7

- Kiely J.L, McNicholas WT. Cardiovascular risk factors in patients with obstructive sleep apnoea syndrome. Eur Respir J 2000;16:128-33

- Knuistingh Neven A, Middelkoop HAM, Kemp B, Kamphuisen HAC, Springer MP. The prevalence of clinically significant sleep apnoea syndrome in the Netherlands. Thorax 1998;53:638-42

- Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993;147(4):887-95

- Krieger J. Long-term compliance with nasal continuous positive airway pressure (CPAP) in obstructive sleep apnea patients and nonapneic snorers. Sleep 1992;15(6 Suppl):S42-6

- Kuhlo W, Doll E, Franck MC. Successful management of Pickwickian syndrome using long-term tracheostomy. Dtsch Med Wochenschr 1969;94(24):1286-90

- Kushida CA, Littner MR, Hirshkowitz M, Morgenthaler TI, Alessi CA, Bailey D, Boehlecke B, Brown TM, Coleman J Jr, Friedman L, Kapen S, Kapur VK, Kramer M, Lee-Chiong T, Owens J, Pancer JP, Swick TJ, Wise MS; American Academy of Sleep Medicine. Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. Sleep 2006;29(3):375-80

- Lavie L, Vishnevsky A, Lavie P. Evidence for lipid peroxidation in obstructive sleep apnea. Sleep 2004; 27: 123-8

- Lavie P. Mortality in sleep apnoea syndrome: a review of the evidence. Eur Respir Rev 2007;16:203-10

- 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;127:230-4

- Li KK, Powell NB, Riley RW, Troell RJ, Guilleminault C. Long-term results of maxillomandibular advancement surgery. Sleep Breath 2000;4(3):137-40

- Lim J, Lasserson TJ, Fleetham J, Wright JJ. Oral appliances for obstructive sleep apnoea (Review). Cochrane Database Syst Rev 2009;3:CD004435

- Littner MR, Kushida C, Wise M, Davila DG, Morgenthaler T, Lee-Chiong T, Hirshkowitz M, Loube DL, Bailey D, Berry RB, Kapen S, Kramer M. Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. Sleep 2005;28(1):113-21

- Lloberes P, Levy G, Descals C, Sampol G, Roca A, Sagales T, de la Calzada MD. Self-reported sleepiness while driving as a risk factor for traffic accidents in patients with obstructive sleep apnoea syndrome and in non-apnoeic snorers. Respir Med 2000;94:971-6

- Lojander J, Maasilta P, Partinen M, Brandler PE, Salmi T, Lehtonen H. Nasal-CPAP, surgery, and conservative management for treatment of obstructive sleep apnea syndrome. A randomized study. Chest 1996;110(1):114-9

- Marin JM, Carrizo SJ, Vicente E, Agusti AGN. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea syndrome with or without treatment with continuous positive airway pressure; an observational study. Lancet 2005;365:1046-53

- Marti S, Sampol G, Muñoz X, Torres F, Roca A, Lloberes P, Sagalés T, Quesada P, Morell F. Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J 2002;20:1511-18

- Maurer JT, Stuck BA, Hein G, Verse T, Hörmann K. Treatment of obstructive sleep apnea with a new vest preventing the supine position. Dtsch Med Wochenschr 2003;128(3):71-5

- McNicholas WT, Bonsignore MR. Sleep apnoea as an independent risk factor for cardiovascular disease: current evidence, basic mechanisms and research priorities. Review. Eur Respir J 2007; 29:156-78

- Meslier N, Gagnadoux F, Giraud P, Person C, Ouksel H, Urban H, Racineux JL. Impaired glucose-insulin metabolism in males with obstructive sleep apnoea syndrome. Eur Respir J 2003;22:156-60

- Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. Am J Respir Crit Care Med 2001;163:1457-61

- Meurice JC, Dore P, Paquereau J, Neau JP, Ingrand P, Chavagnat JJ, Patte F. Predictive factors of long-term compliance with nasal continuous positive airway pressure treatment in sleep apnea syndrome. Chest 1994;105(2):429-33

- Morgenthaler TI, Aurora RN, Brown T, Zak R, Alessi C, Boehlecke B, Chesson Jr AL, Friedman L, Kapur V, Maganti R, Owens J, Pancer J, Swick TJ. Practice parameters for the use of autotitrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome: An update for 2007. An American academy of sleep medicine report. Sleep 2008;31(1):141-7

- Nguyen AT, Baltzan MA, Small D, Wolkove N, Guillon S, Palayew M. Clinical reproducibility of the Epworth Sleepiness Scale. J Clin Sleep Med 2006;2(2):170-4

- Nino-Murcia G, McCann CC, Bliwise DL, Guilleminault C, Dement WC. Compliance and side effects in sleep apnea patients treated with nasal continuous positive airway pressure. West J Med 1989;150(2):165-9

- Oksenberg A, Silverberg DS, Arons E, Radwan H. Positional vs nonpositional obstructive sleep apnea patients. Chest 1997;112:629-39

- Oksenberg A, Silverberg DS, Offenbach D, Arons E. Positional therapy for obstructive sleep apnea patients: A 6-month follow-up study. Laryngoscope 2006;116:1995-2000

- Oltmanns KM, Gehring H, Rudolf S, Schultes B, Rook S, Schweiger U, Born J, Fehm HL, Peters A. Hypoxia causes glucose intolerance in humans. Am J Respir Crit Care Med 2004;169:1231-7

- Osler W. The Principles and Practice of Medicine, 4th edition 1901;439

- Osler W. The Principles and Practice of Medicine, 6th edition 1901

- Pepin JL, Krieger J, Rodenstein D, Cornette A, Sforza E, Delguste P, Deschaux C, Grillier V, Levy P. Effective compliance during the first 3 months of continuous positive airway pressure. A European prospective study of 121 patients. Am J Respir Crit Care Med 1999;160(4):1124-9

- Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 2000;284(23):3015-21

- Petit FX, Pépin JL, Bettega G, Sadek H, Raphaël B, Lévy P. Mandibular advancement devices. Rate of contraindications in 100 consecutive obstructive sleep apnea patients. Am J Respir Crit Care Med 2002;166:274–8

- Philips BG, Narkiewicz K, Pesek CA, Haynes WG, Dyken ME, Somers VK. Effects of obstructive sleep apnea on endothelin-1 and blood pressure. J Hypertens 1999;17:61-6

- Pieters T, Collard P, Aubert G, Dury M, Delguste P, Rodenstein DO. Acceptance and long-term compliance with nCPAP in patients with obstructive sleep apnoea syndrome. Eur Respir J 1996;9(5):939-44

- Pirsig W, Verse T. Long-term results in the treatment of obstructive sleep apnea. Eur Arch Otorhinolaryngol 2000;257:570-7

- Powell NB, Riley RW, Guilleminault C. Radiofrequency tongue base reduction in sleep-disordered breathing: a pilot study. Otolaryngol Head Neck Surg 1999;120:656-64

- Prinsell JR.Maxillomandibular Advancement (MMA) in a Site-Specific Treatment Approach for Obstructive Sleep Apnea: A Surgical Algorithm. Sleep Breath 2000;4(4):147-54

- Popescu G, Latham M, Allgar V, Elliott MW. Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. Thorax 2001;56(9):727-33

- Punjabi NM, Polotsky VY. Disorders of glucose metabolism in sleep apnea. J Appl Physiol 2005: 99: 1998-2007

- Punjabi NM, Sorkin JD, Katzel LI, Goldberg AP, Schwartz AR, Smith PL. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. Am J Respir Crit Care Med 2002;165:677-82

- Rabelo FA, Braga A, Küpper DS, De Oliveira JA, Lopes FM, de Lima Mattos PL, Barreto SG, Sander HH, Fernandes RM, Valera FC. Propofol-induced sleep: polysomnographic evaluation of patients with obstructive sleep apnea and controls. Otolaryngol Head Neck Surg 2010;142(2):218-24

- Rauscher H, Formanek D, Popp W, Zwick H. Self-reported vs measured compliance with nasal CPAP for obstructive sleep apnea. Chest 1993;103(6):1675-80

- Resta O, Guido P, Picca V, Scarpelli F, Foschino MP. The role of the expiratory phase in obstructive sleep apnoea. Respir Med 1999;93(3):190-5

- Riley RW, Powell NB, Li KK, Weaver EM, Guilleminault C. An adjunctive method of radiofrequency volumetric tissue reduction of the tongue for OSAS. Otolaryngol Head Neck Surg 2003;129:37-42

- Riley RW, Powell NB, Guilleminault C. Inferior sagittal osteotomy of the mandible with hyoid myotomy-suspension: a new procedure for obstructive sleep apnea. Otolaryngol Head Neck Surg 1986;94(5):589-93

- Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea and the hyoid: a revised surgical procedure. Otolaryngol Head Neck Surg 1994;111(6):717-21

- Riley RW, Powell NB, Guilleminault C, Ware W. Obstructive sleep apnea syndrome following surgery for mandibular prognathism. J Oral Maxillofac Surg 1987;45(5):450-2

- Rodriguez-Bruno K, Goldberg AN, McCulloch CE, Kezirian EJ. Test-retest reliability of drug-induced sleep endoscopy. Otolaryngol Head Neck Surg 2009;140(5):646-51

- Sadaoka T, Kakitsuba N, Fujiwara Y, Kanai R, Takahashi H. The value of sleep endoscopy in the evaluation of patients suspected sleep-related breathing disorders. Clin Otolaryngol 1996;21:485-9

- Sanders MH, Gruendl CA, Rogers RM. Patient compliance with nasal CPAP therapy for sleep apnea. Chest 1986;90(3)330-3

- Schäfer H, Ewig S, Hasper E, Lüderitz B. Failure of CPAP therapy in obstructive sleep apnoea syndrome: predictive factors and treatment with bilevel-positive airway pressure. Respir Med 1998;92(2):208-15

- Sin DD, Mayers I, Man GC, Pawluk L. Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study. Chest 2002;121(2):430-5

- Smith I, Lasserson TJ Pressure modification for improving usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea (Review). Cochrane Database Syst Rev 2009;4:CD 003531

- Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter E. Sleep loss: a novel risk factor for insulin resistance and type 2 diabetes. J Appl Physiol 2005;99:2008-19

- Stigter H, Lammers GJ, Rooyackers JM. Slaapstoornissen en rijgeschiktheid. Herziening van de regelgeving. Ned Tijdschr Geneeskd 2009;153:A690

- Stuck BA, Maurer JT, Verse T, Hormann K. Tongue base reduction with temperature-controlled radiofrequency volumetric tissue reduction for treatment of obstructive sleep apnea syndrome. Acta Otolaryngol 2002;122:531-6.

- Stuck BA, Köpke J, Maurer JT, Verse T, Eckert A, Bran G, Duber C, Hormann K. Lesion formation in radio frequency surgery of the tongue base. Laryngoscope 2003;113:1572-6

- Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1981;1(8225):862-5

- Thatcher GW, Maisel RH. The long-term evaluation of tracheostomy in the management of severe obstructive sleep apnea. Laryngoscope 2003;113(2):201-4

- Vaartjes M, Strijers RLM, de Vries N. Posterior nasal packing and sleep apnes. Am J Rhinol 1992;6:71-4

- Veale D, Chailleux E, Hoorelbeke-Ramon A, Reybet-Degas O, Humeau-Chapuis MP, Alluin-Aigouy F, Fleury B, Jonquet O, Michard P. Mortality of sleep apnoea patients treated by nasal continuous positive airway pressure registered in the ANTADIR observatory. Association Nationale pour le Traitement A Domicile de l'Insuffisance Respiratoire chronique (ANTADIR). Eur Respir J 2000;15:326-31

- Verse T, Maurer JT, Pirsig W. Effect of nasal surgery on sleep-related breathing disorders. Laryngoscope 2002;112(1):64-8

- Waldhorn RE, Herrick TW, Nguyen MC, O'Donnell AE, Sodero J, Potolicchio SJ. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest 1990;97(1):33-8

- Wetmore SJ, Scrima L, Hiller FC. Sleep apnea in epistaxis patients treated with nasal packs. Otolaryngol Head Neck Surg 1988;98(6):596-9

- Woodson BT, Nelson L, Mickelson S, Huntley T, Sher A. A multi-institutional study of radiofrequency volumetric tissue reduction for OSAS. Otolaryngol Head Neck Surg 2001;125:303-11

- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328(17):1230-5

- Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 1997;20(9):705-6

- Young T, Blustein J, Finn L, Palta M. Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. Sleep 1997;20(8):608-13

List of publications

Articles

De Kleijn DPV, Sluijter JPG, Smit J, Velema E, Richard W, Schoneveld AH, Pasterkamp G, Borst C. Furin and membrane type-1 metalloproteinase mRNA levels and activation of metalloproteinase-2 are associated with arterial remodeling. *FEBS Lett*. 2001 Jul 13;501(1):37-41.

Vink A, Schoneveld AH, Richard W, de Kleijn DPV, Falk E, Borst C, Pasterkamp G. Plaque burden, arterial remodeling, and plaque vulnerability: determined by systemic factors? *J Am Coll Cardiol*. 2001 Sep;38(3):718-23.

Sluijter JPG, Smit JP, Schoneveld AH, de Kleijn DPV, Velema E, Richard W, Pasterkamp G, Borst C. Increased furin and membrane type-1 metalloproteinase mRNA levels and activation of metalloproteinase 2 are associated with arterial remodelling during sustained flow changes. *Europ. Heart Journal abstr. suppl*. 2001 Sep;22:382

Richard W, Bruintjes TjD, Oostenbrink P, Leeuwen van RB. Efficacy of the Epley maneuver for posterior canal BPPV: a long-term, controlled study of 81 patients. *Ear Nose Throat J.* 2005 Jan;84(1):22-5

Richard W, den Herder C, de Vries N. Surgical treatment of obstructive sleep apnea syndrome. *Ned Tijdschr Geneeskd*. 2005 May 28;149(22):1193-6. Dutch

Richard W, Hessel NS, de Vries N. Response to Oksenberg. *Clin Otolaryngol.* 2005 Oct 30;5:483-4

Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N. The role of sleep position in obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol.* 2006 Oct;263(10):946-50

Richard W, Kox D, den Herder C, van Tinteren H, de Vries N. One stage multilevel surgery (uvulopalatopharyngoplasty, hyoid suspension, radiofrequent ablation of the tongue base with/without genioglossus advancement), in obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol.* 2007 Apr;264(4):439-44

Richard W, Venker J, den Herder C, Kox D, van den Berg B, Laman M, van Tinteren H, de Vries N. Acceptance and long-term compliance of nCPAP in obstructive sleep apnea. *Eur Arch Otorhinolaryngol*. 2007 Sep;264(9):1081-6

Richard W, Snow GB. Een knobbeltje in de wang. *Ned Tijdschr KNO-Heelk.* 2008;14(2):93-5

van den Broek E, Richard W, van Tinteren H, de Vries N. UPPP combined with radiofrequency thermotherapy of the tongue base for the treatment of obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol*. 2008 Nov;265(11):1361-5

Richard W, Timmer F, van Tinteren H, de Vries N. Complications of hyoid suspension in the treatment of obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol*. 2011 Apr;268(4):631-5

Maanen JP, Richard W, van Kesteren ER, Ravesloot MJL, Laman DM, Hilgevoord AAJ, de Vries N. Evaluation of a new simple treatment for positional sleep apnea patients. *J Sleep Res.* 2011 Oct 22. [Epub ahead of print]

Bookchapters

Richard W, Venker J, den Herder C, Kox D, Vries N. Analysis of nCPAP failures. In: Sleep apnea and snoring. Surgical and non-surgical therapy. Friedman. 2009;chapter 10:69-71

de Vries N, Richard W, Kox D, den Herder C. Multilevel surgery (hyoid suspension, radiofrequent ablation of the tongue base uvulopalatopharyngoplasty) with/without genioglossus advancement. In: Sleep apnea and snoring. Surgical and non-surgical therapy. Friedman. 2009;chapter 50:312-20

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Curriculum Vitae

Wietske Richard was born in Amersfoort on May 7th, 1978. After graduating from secondary school in 1996, at the Scholengemeenschap de Amersfoortse Berg in Amersfoort, she started medical school at the Erasmus University in Rotterdam. She obtained her medical degree in 2002. After her medical training she worked as a resident at the emergency room of the Flevohospital in Almere. In 2004 she started as a resident at the department Otolaryngology/ Head and Neck Surgery in the Sint Lucas Andreas hospital in Amsterdam where she also commenced her PhD studies under direct supervision of Dr N. de Vries. As part of her PhD studies she investigated different aspects of obstructive sleep apnea syndrome. In March 2006 she started her ENT (Ear, Nose, Throat) residency at the Academic Medical Centre in Amsterdam, during which she completed this thesis.
She lives in Soest with Maurice Smeeing and is the mother of a son and a daughter, named Willem and Fien. In September they expect their third child.