The potential of novel treatment options for position-dependent obstructive sleep apnea syndrome

Towards a better appreciation of sleep position

Johan Peter van Maanen

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De potentie van nieuwe behandelingen van positie-afhankelijk obstructief slaap apneu syndroom

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Aan mijn ouders

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GENERAL INTRODUCTION AND OUTLINE OF THESIS

"I am informed that Dionysius the Heracleote, son of Clearchus the Tyrant, through daily Gluttony and intemperance, increased to an extraordinary degree of Corpulency and Fatness, by reason whereof he had much adoe to take breath. The Physicians ordered for remedy of this inconvenience, that Needles should be made very long and small, which when he fell into sound sleep should be thrust through his sides into his belly. Which office his Attendants performed, and till the Needle had passed quite through the fat, and came to the flesh it self, he lay like a stone; but when it came to the firm flesh, he felt it and awaked."[1]

OSAS

Dionysius was one of the first reported sufferers from obstructive sleep apnea syndrome (OSAS).[1] OSAS has been clinically recognized almost 40 years ago[2] and although medical research has been focussing on the pathophysiology and treatment of OSAS for approximately 30 years now, it is very likely that the disease is as old as obesity in man. OSAS is the most prevalent type of sleep-disordered breathing, a disease spectrum also including central sleep apnea syndrome and hypoventilation-hypoxemic syndrome. OSAS is characterized by a decrease or complete halt in airflow despite an ongoing effort to breathe. This leads to partial reductions (hypopneas) and complete pauses (apneas) in breathing that last at least 10 seconds during sleep and that occur more than five times per hour of sleep. OSAS is defined as:

A. Excessive daytime sleepiness that is not better explained by other factors;

B. Two or more of the following that are not better explained by other factors:

- choking or gasping during sleep,
- recurrent awakenings from sleep,
- unrefreshing sleep,
- daytime fatigue,
- impaired concentration; and/or

C. Overnight monitoring demonstrates five or more obstructed breathing events per hour during sleep. These events may include any combination of obstructive apneas, hypopneas or respiratory effort related arousals (Table 1).

To suffer from OSAS one should fulfil criterion A or B, plus criterion C.[3]

The severity of OSAS is expressed in the apnea hypopnea index (AHI): the mean number of total events per hour of sleep as measured by polysomnography (PSG) with thresholds for adults being a minimum of 5, 15 and 30 events per hour for mild, moderate and severe levels of OSAS.

AHI thresholds in children are different. This thesis focuses only on adult patients.

Table 1 - Definition of apnea, hypopnea and respiratory effort-related arousal (RERA) according to the American Academy of Sleep Medicine recommendations.[4]

Apnea*	An episode with a greater than 90% reduction of oronasal airflow; obstructive if respiratory effort is present, central if no respiratory effort is present.
Hypopnea*	An episode of greater than 30% reduced oronasal airflow for 10 sec or more accompanied by a decrease of 4% or more of the arterial oxyhemoglobin saturation.
RERA*	A sequence of breaths characterized by increasing respiratory effort or flattening of the nasal pressure waveform leads to an arousal from sleep and does not meet the criteria for apnea or hypopnea.

* By definition an event has to last for at least 10 seconds.

Position-dependent snoring and position-dependent OSAS (POSAS)

At least for decades, but more likely for centuries, it has been recognized by patients and their bed partners that the loudness of snoring is worse when in the supine position.[5] Simple snoring without apnea is often louder and more frequent in the supine sleeping position.[6] Approximately 66% of non-apneic snorers are position-dependent.[7] The distinction between simple snoring and POSAS is an important one in the context of body position and the goals of treatment. The existence of position-dependent OSAS (POSAS) has been described by Cartwright in 1984[8] and is defined as an AHI greater than 5 per hour sleep and an AHI in the supine position twice as high or more when compared to the AHI in nonsupine positions together with subjective complaints.

Other definitions for POSAS have been suggested:

- an AHI of fewer than 5 events per hour sleep while in the non-supine position as well as a decrease in the AHI by more than 50%[9,10]
- a supine AHI ≥ 10, together with a lateral AHI < 10 per hour sleep[11]
- overall AHI ≥ 15 per hour sleep, supine AHI ≥ twice the non-supine AHI; ≥ 20 minutes of sleep in supine and non-supine postures and non-supine AHI < 15 per hour sleep.[12]

Cartwright's definition is the most common definition for POSAS used today and the one used in this thesis.

Prevalence and risk factors

Research in the United States of America (USA) has estimated that the prevalence rates of moderate to severe OSAS are 10% among 30-49-year-old men, 17% among 50-70-year-old men, 3% among 30-49-year-old women and 9% among 50-70-year-old women.[13] Earlier research has shown that a large proportion of patients suffering from moderate to severe OSAS remains undiagnosed. Research in the USA has shown that in particular people with lower socioeconomic status, non-whites and women are often undiagnosed.[14] Factors that predispose to OSAS include male gender, obesity, anomalies of the upper airway (anatomical, functional or both), age > 60 years, smoking and alcohol consumption.[15] Obesity could increase the likelihood of airway collapse, since fat can be deposited in surrounding structures, thereby directly affecting the anatomy of the upper airway. MRI studies

have shown that fat is deposited within the tissue of the tongue, which could impair function of the genioglossus muscle and could suffer more from gravitational forces.[16] Obesity might also increase the risk of obstructive sleep apnea via effects on lung volumes and stability of respiratory control. The male to female ratio is 11.1:1 for all severities of OSAS,[17] and 2.6:1 in mild to moderate OSAS.[18] The mechanism of how male sex predisposes to OSAS is not so clear.[19] Women tend to gain weight less centrally than do men, and this pattern probably results in men having stored more fat in upper airway structures and the abdomen compared to women.[20] However, anatomical studies confirm that men seem to have equally or larger sized pharyngeal airway cross-sectional areas than women, suggesting that differences in fat deposition might not greatly impair airway anatomy. In a case series carried out in a university hospital sleep disorders clinic comprising almost 4000 patients it was found that men had a higher AHI than women even after controlling for age, body mass index (BMI) and neck circumference.[21] More than 55% of OSAS patients suffer from position-dependent OSAS (POSAS).[22,23] In the Asian population its prevalence is even higher: between 67 and 75% of OSAS patients in Asia suffer from POSAS.[24,25] POSAS correlates negatively with BMI and OSAS severity.[9]

Pathophysiology and symptoms

OSAS can be seen as a result of abnormal anatomy (crowding of the upper airway) superimposed on physiologic or excessive reduction of muscle tone during sleep. In OSAS, an imbalance exists between forces dilating and occluding the pharynx during sleep. The muscle tone supporting the airway lumen is too low and the inspiratory suction force together with the pressure of the surrounding tissues is too high. By definition, and as a result of a physiological loss of muscle tone of the pharyngeal muscles, this disorder occurs only during sleep. Disturbances in sleep-related gas exchange lead to oxygen desaturation, hypercapnia, and sleep fragmentation. This often leads to daytime and nighttime symptoms (Table 2).

Table 2 - Some of the symptoms and signs of obstructive sleep apnea syndrome.

Daytime	Nighttime
Sleepiness	Snoring
Impaired concentration	Observed apnea
Irritability	Choking
Depression symptoms	Sweating
Decreased libido	Nocturia

Breathing cessation or reduction in breathing results in hypoventilation and consequent hypoxemia, changes in autonomic nervous system tone possibly leading to bradycardia and other arrhythmias during sleep and systemic hypertension. To start breathing again, most patients awaken briefly, which re-establishes ventilation. These patients can have hundreds of arousals each night, resulting in repetitive cardiorespiratory changes during sleep or unstable fragmented sleep. These two consequences result in the clinical features at presentation, such as neural symptoms like daytime sleepiness. The cardiorespiratory changes result in an increased risk of arterial hypertension, coronary artery disease, and stroke.[26]

Accurate and timely diagnosis for patients with OSAS is imperative since severe OSAS increases the risk of morbidity and mortality from cardiovascular disease[27,28] and traffic accidents.[29-31]

Clinical assessment

A thorough history preferably in the presence of and with participation of the bedpartner and physical examination are an integral part of the initial evaluation of patients with suspected OSAS. History focuses on OSAS symptoms, sleep history, general medical information, including surgical history, prior OSAS treatment, comorbidities, occupation, alcohol and tobacco consumption and medication use. The severity of daytime sleepiness is evaluated using the Epworth Sleepiness Scale (ESS), a self-administered questionnaire that provides a measurement of the subject's general level of daytime sleepiness (Table 3). An observational study of 180 adults showed that among healthy subjects the ESS is 6, that a score of 16 or higher is associated with narcolepsy, idiopathic hypersomnia, or moderate to severe OSAS and that a score of 10 or more is consistent with excessive sleepiness.[32] However, the strength of the correlation between the ESS and objective measures of sleepiness, i.e. multiple sleep latency test and maintenance of wakefulness test, remains controversial with multiple studies indicating little or no correlation between the tests.[33-37] Physical examination includes body mass index (BMI), neck circumference, tongue size, tonsil size, position of the soft palate, length of the uvula, mandible position or size and dental status.[38] However, the predictive value of these clinical tools is poor with a sensitivity and specificity of subjective clinical impression of 60% and 63% respectively. Taken together, history, physical examination and clinician impression were only able to predict OSAS in about 50% of patients in an observational study of 600 patients.[39] Other studies also showed that history and physical examination alone cannot reliably diagnose OSAS[40-42] and the gold standard for diagnosing OSAS remains polysomnography (PSG), preferably the attended overnight polysomnogram.[3]

Table 3 - The Epworth Sleepiness Scale.[32]

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you.

0 = would never doze
1 = slight chance of dozing
2 = moderate change of dozing
3 = high chance of dozing

Situation	Chance of dozing
Sitting and reading	____
Watching TV	____
Sitting, inactive in a public place (e.g. a theatre or a meeting)	____
As a passenger in a car for an hour without a break	____
Lying down to rest in the afternoon when circumstances permit	____
Sitting and talking to someone	____
Sitting quietly after a lunch without alcohol	____
In a car, while stopped for a few minutes in the traffic	____

Polysomnography (PSG) and polygraphy (PG)

Full-night polysomnography (PSG) requires recording of the following physiologic signals: electroencephalogram (EEG), electrooculogram (EOG), chin electromyogram, airflow, oxygen saturation, respiratory effort, and electrocardiogram (ECG) or heart rate. Additional parameters include body position and leg EMG derivations. Anterior tibialis EMG is useful to assist in detecting movement arousals and may have the added benefit of assessing periodic limb movements, which coexist with sleep-related breathing disorders in many patients.[43] The parameters, settings, filters, technical specifications, sleep stage scoring and event scoring should be done in accordance with the AASM Manual for the Scoring of Sleep and Associated Events.[4] The frequency of obstructive events is reported as an apnea + hypopnea index (AHI) or respiratory disturbance index (apnea + hypopnea + RERA index, RDI). In the Netherlands AHI is used more often than RDI and OSAS is confirmed when an AHI equal to or greater than 5 is found.[44]

Despite the clear influence of the supine position on sleep-disordered breathing, few data exist on how body position should be recorded and the accuracy of currently available body position sensors is unknown. In earlier day, the effect of body position on sleep disordered breathing was evaluated using direct observation and recording overnight. Nowadays, most body position sensors are placed on the lower part of the sternum, usually in or attached to a band strapped around the chest. Portable monitors (polygraphy) to diagnose sleep disordered breathing have been classified earlier[45] and can be used in select cases. Unfortunately, most portable monitors are unable to accurately report body position or sleep time.[46]

OSAS treatment

Since OSAS is known to increase the risk of morbidity and mortality from cardiovascular disease[27,28] and traffic accidents,[29-31] adequate OSAS treatment is of key importance.

Conservative measures

Standard recommendations in the treatment of sleep-disordered breathing include weight loss in overweight patients (BMI>25 kg/m^2), avoidance of alcohol and sedatives, reduction and preferably cessation of smoking and maintenance of a regular sleep rhythm. In OSAS patients with a BMI>35 who fail to lose weight following dietary modification and exercise, bariatric surgery (Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy, or biliopancreatic diversion) should be considered since a meta-analysis studying 3 randomized controlled trials, 11 controlled trials and 55 case series has reported significant improvement of OSAS severity in obese patients following bariatric surgery.[47]

Positional therapy (PT)

Since more than 55% of OSAS patients suffer from POSAS, preventing patients from sleeping in a supine position will be beneficial to the severity of their OSAS. The so-called “tennis ball technique” has been the first type of positional therapy, documented in 1984.[5] Later, other types of positional therapy, all variations on the same theme, rather bulky masses placed in one’s back, have been developed and investigated.[48-54] Positional therapy, consisting of a bulky mass placed in one’s back, has been shown to be as effective as CPAP in a group of mild to moderate POSAS patients.[10,55]

Long-term compliance, however, is low with less than 10% of patients reporting continued use approximately 2,5 years after prescription. Side effects and reasons why patients stopped using positional therapy were discomfort with most often problems with turning from side to side, displacement of the device during the night, lack of sleep quality improvement, back ache, shoulder problems, skin irritation and inability of the device from preventing one to sleep in supine position.[56] Contraindications for positional therapy are physical problems causing inability to sleep on the side.

Continuous positive airway pressure (CPAP)

Described for the first time in 1981,[57] nasal CPAP is regarded as the gold standard treatment of moderate to severe OSAS. It has been shown to improve the functional outcome of sleepy patients with mild and moderate OSAS.[58] CPAP most likely exerts its effects by a positive pharyngeal transmural pressure so that the intraluminal pressure exceeds the surrounding pressure. Furthermore it causes an increase in end-expiratory lung volume.[59] In a Cochrane meta-analysis CPAP has shown to significantly effective reduce AHI as well as improve quality of life, cognitive function and objective and subjective measures of sleepiness.[60]

CPAP's clinical effectiveness, however, is often limited by low patient acceptance, poor tolerance and subsequently a suboptimal CPAP compliance. It's a clinical reality that CPAP compliance can be cumbersome. Patients either tolerate CPAP very well, or do not tolerate it at all. Reportedly, 29-83% of patients are non-adherent to treatment, when adherence is defined as at least 4 hours of nightly CPAP use.[61] Patients likely to maintain long-term adherence include those who snore heavily and those who have severe OSA.[62] To improve CPAP compliance more support and care is needed, especially intensive early interventions e.g. at one month could improve long-term compliance.[63] Side effects of CPAP use consist of nasal congestion or mouth/airway dryness, eye problems because of a leaking mask, claustrophobia, noise problems, facial soreness or skin irritation from the mask and mask fit problems for example trouble keeping the mask in place. One study, carried out in China, Australia and New Zealand found the following side effects (in decreasing prevalence percentage): dry mouth (42%), nasal symptoms (31%), mask fit or leak problems (23%), soreness or skin irritation (17%), noise problems (10%), eye problems (9%), claustrophobia (1%).[63]

Mandibular repositioning appliance (MRA)

Mandibular repositioning appliances (MRAs) have shown to be a highly effective treatment for selected OSAS patients. Especially patients with snoring or mild to moderate OSAS seem to benefit from this treatment regimen.[64] MRA therapy is increasingly prescribed as a non-invasive first-line alternative to CPAP, especially in aforementioned patients.[65] MRAs seem to exert their effects by increasing the lumen and stabilization of the upper airway. Especially the lateral dimensions at the level of the velopharynx seem to be widened whilst using MRA therapy.[66] MRA treatment has a higher self-reported compliance rate and a higher patient preference when compared to CPAP therapy.[67,68]

There is growing evidence that MRA therapy could also be effective at improving the adverse health consequences of OSAS.[67,69] Objective usage data and compliance for MRA, until recently,[70] have been difficult to collect and have been limited to subjective self-report. However, recently it was shown

that objective and subjective long-term MRA compliance data show a high correspondence and long-term regular use was found to be 83% in a group of 51 patients with a follow-up of one year.[71] Side effects from the appliance include discomfort, salivation problems and orthodontic effects on teeth and jaws resulting in discontinuation of treatment or poor compliance for about 20–50% of initially treated patients.[72,73]

Contraindications for MRA treatment include insufficient teeth to support the device, a limited capacity for mandibular protrusion, presence of periodontal disease and temporomandibular dysfunction. Petit et al. reported a study of 100 consecutive OSAS patients in which 34% suffered from these dental contraindications to MRA therapy, thereby limiting the scope of this type of treatment.[74]

Surgery for obstructive sleep apnea syndrome

Nasal surgery has no role as primary treatment in OSAS patients. Multiple studies found statistically non-significant reductions or even increases in AHI in OSAS patients primarily treated with nasal surgery, including inferior turbinate reduction, septoplasty and/or functional endoscopic sinus surgery.[75-77] However, in patients who cannot tolerate their CPAP treatment because of nasal breathing problems it can help increase their CPAP compliance.[78]

Different types of surgery at the level of the soft palate exist. The in 1981 introduced uvulopalatopharyngoplasty (UPPP) by Fujita et al. still is the most commonly performed procedure in OSAS patients.[79] It aims to increase the retropalatal lumen and reduce the collapsibility of the pharynx, by resection of the free edge of the uvula and soft palate, in combination with a tonsillectomy. A modification of this procedure is the Z-palatoplasty (ZPP) and can be used in earlier tonsillectomised patients.[80] More palatal surgical procedures exist, but this is beyond the scope of this thesis. In a meta-analysis by Sher et al, an overall response rate of 40.7% was reported with response defined as a 50% decrease in the respiratory disturbance index (RDI) and a postoperative RDI of 20 per hour, or as a 50% decrease in the apnea index (AI) and a postoperative AI of 10 per hour in patients treated with UPPP alone, regardless of site of obstruction. In patients with suspected hypopharyngeal obstruction the response rate was 5.3%, whilst in patients with suspected palatal narrowing alone, the response rate increased to 52.3%.[81]

Procedures aiming to increase the retrolingual space comprise of a large variety of procedures, e.g. radiofrequent ablation (RFTB),[82] genioglossus advancement,[83] hyoidthyroidpexia (HTP),[84] midline glossectomy[85] and hypoglossal nerve stimulation.[86] RFTB and HTP up to now have been the workhorses in tongue base surgery. In a meta-analysis from 2006 it was shown that successful AHI reductions for RFTB are widely ranging from 20-83% and for HTP from 22-77% (level IV evidence). Successful AHI reduction was defined as a reduction in AHI of 50% or more and an AHI of less than 20 events per hour sleep postoperative.[87]

Side effects of palatal procedures include: dysphagia, globus, prolonged angina, bleeding and infection, speech and taste disorders, velopharyngeal incompetence and nasopharyngeal stenosis. Side effects of base of tongue procedures include: prolonged angina, globus, bleeding and infection and dysphagia. Maxillomandibular advancement (MMA), a procedure routinely performed to correct dentofacial

dysgnathia, has been shown to be a highly effective treatment for OSAS patients. It results in widening of the pharynx and enhances the tension of the soft tissues, reducing the collapsibility and obstruction of the pharynx.[88] Reported long-term success rates concerning AHI decrease are 80-90%.[89,90] Complications of MMA include hypesthesia of the lower lip, local infection, bleeding, malocclusion and temporomandibular joint disorders.[88]

Tracheostomy, a last resort surgical solution for severe OSAS patients, has been described as an OSAS treatment by various authors starting around 1969.[91] Since a tracheostomy completely bypasses the collapsing part of the OSAS patient's airway it is the most successful treatment option, regardless of a patient's BMI.[92] Some of the side effects and complications of tracheostomy include: bleeding, infection, frequent coughing up of mucus, formation of granulation tissue, mucous plugging of the tracheostomy tube, aspiration, pneumonia. Furthermore a tracheostoma is associated with psychosocial problems and inconvenience.[92,93]

Upper airway assessment

Goals of upper airway assessment include a better insight into the complex pathophysiology of upper airway collapse and improvement of treatment success rates by selecting the most appropriate therapeutic options for individual patients.[94] Different techniques evaluating the level(s) of obstruction in the upper airway exist including: x-ray cephalometry, CT or MRI scan of the head and neck, flow and pressure measurements, awake flexible endoscopy, sleep endoscopy during natural sleep and drug-induced sleep endoscopy. For non-CPAP treatment selection in patients with sleep-disordered breathing, drug-induced sleep endoscopy (DISE) is gaining momentum.[95] DISE has been shown to improve treatment outcome. [96-98]

Drug-induced sleep endoscopy (DISE)

The DISE technique has been extensively reported previously.[99] Drugs most commonly used for DISE are propofol and/or midazolam. Some use propofol only; others use midazolam only. Others start with midazolam and continue with propofol.

Anaesthetic depth is of key importance. The target depth of sedation is the transition from consciousness to unconsciousness (loss of response to verbal stimulation). Because individuals have different susceptibilities to midazolam/propofol, the required dosage can vary widely. Slow stepwise induction is required to avoid oversedation.

Different methods for assessment of level and type of upper airway collapse have been described in the literature.[95] In the Netherlands DISE is scored using the VOTE-classification.[100] Velum, oropharynx (including tonsils), tongue base and epiglottis are evaluated. Distinction in configuration is made between anteroposterior, lateral or concentric, depending on the level of obstruction. The degree of airway narrowing is defined as either none (0) (0–50 % obstruction), partial (1) (50–75 % obstruction) or complete (2) (≥75 % obstruction). During DISE, a chinlift and a jaw thrust is performed and the different VOTE-levels are assessed once again to evaluate whether a MRA is a viable treatment option.

OUTLINE OF THESIS

This thesis aims to discuss the following research questions:

1. Is position recording using a trunk position sensor in overnight sleep studies sufficient?
2. What are the short-term effects of novel positional therapies consisting of devices capable of producing a vibrational stimulus upon detection of the supine sleep position?
3. How is the long-term compliance and effectiveness of this novel positional therapy?
4. Can positional therapy increase treatment efficacy in patients in whom OSAS surgery is considered or already performed?

Almost all currently available body position sensors are worn in a band strapped around the chest. Chapter 1 describes measurements of head position and the influence of head position on the occurrence of nocturnal respiratory events in a cohort of clinically suspected OSAS patients.

Most types of positional therapy (PT) consist of tennis balls or other bulky masses placed in one's back. Chapter 2 describes the effects of a novel type of PT, a neck worn device aiming to prevent POSAS patients from sleeping in supine position.

Chapter 3 gives an overview of currently investigated types of PT as well as more insight in POSAS patients in general.

In chapter 4 another novel type of PT, the Sleep Position Trainer (SPT), is demonstrated. Its effects on polysomnographical parameters in a cohort of mild to moderate POSAS patients are shown.

Long-term compliance of PT has been low, due to for example discomfort and inability to prevent one from sleeping in supine position. Results of SPT usage in terms of long-term compliance and prevention of sleeping in supine position are given in chapter 5.

When reporting on treatment outcomes following sleep surgery, the overall AHI is one of the key parameters shown in literature. Success rates of surgery can be influenced by time spent in different sleeping positions. Chapter 6 and 7 give more insight into the effects of body position on outcome of common sleep surgery. In chapter 7 a hypothetical model using an ideal type of PT as single treatment or in addition to palatal surgery is shown aiming to increase efficacy of OSAS treatment.

A summary, conclusions and future perspectives section together with a summary in Dutch is included following chapter 7.

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CHAPTER 1

Quantitative effects of trunk and head position on the apnea hypopnea index in obstructive sleep apnea

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ABSTRACT

Study Objective

To test the hypothesis that head position, separately from trunk position, is an additionally important factor for the occurrence of apnea in obstructive sleep apnea syndrome (OSAS) patients.

Methods

Three hundred patients referred to our department because of clinically suspected OSAS.Patients underwent overnight polysomnography with 2 position sensors: one on the trunk, and one in the mid-forehead.

Results

Of the 300 subjects, 241 were diagnosed with OSAS, based on an AHI >5. Of these patients, 199 could be analyzed for position-dependent OSAS based on head and trunk position sensors (AHI in supine position twice as high as AHI in non-supine positions): 41.2% of the cases were not position dependent, 52.3% were supine position dependent based on the trunk sensor, 6.5% were supine position dependent based on the head sensor alone. In 46.2% of the trunk supine position-dependent group, head position was of considerable influence on the AHI (AHI was >5 higher when the head was also in supine position compared to when the head was turned to the side).

Conclusion

The results of this study confirm our hypothesis that the occurrence of OSAS may also be dependent on the position of the head. Therefore in patients with a suspicion of position-dependent OSAS, sleep recording with dual position sensors placed on both trunk and head should be considered.

INTRODUCTION

Several studies in the past, including a recent study from our group,[1] have demonstrated the effect of body position during sleep on the severity of respiratory disturbances in patients with obstructive sleep apnea syndrome (OSAS). In a large proportion of patients the apnea hypopnea index (AHI) is highest when lying on the back as compared to the other sleeping positions.[2-6] In the hypnogram, this is reflected by a clustering of respiratory events correlated with the change in body position. However, in our patient population, we sometimes encountered hypnograms with this clustering of apnea/hypopnea, but without any clear relation with the recorded body position (or sleep stage). At first we suspected this to be due to a technical imperfection of the position sensor readout. Surprisingly, in the literature we found no clear established research or guidelines on how to record sleeping position most reliably. In some systems, position sensors are integrated in the portable recording device strapped to the chest of the patient. Commonly (and used in our center), position sensors are attached to the elastic bands around either the chest or abdomen used to record respiratory movement. To rule out a sensor displacement, we taped the position sensor directly to the skin at the lower part of the sternum. In a consecutive group of patients, we verified that this gave a much more consistent relation between sensor position readout and actual trunk position and was well tolerated by the patients. Despite this procedural refinement, the frequently observed discrepancy between apnea/hypopnea clustering and body position persisted. We hypothesized that this could be related to the position of the head relative to that of the trunk. This study was conducted to test this hypothesis by performing sleep recordings in subjects suspected of OSAS with dual position sensors placed on both the chest and the head.

Patients

Patients were referred to our department because of clinically suspected OSAS. In total, 300 consecutive adult patients (age >18 years, average 50 years) who underwent overnight polysomnography in our center during the period between July 2008 and June 2009 were included in the study. There were 227 male subjects (mean age 50 years) and 73 females (mean age 49 years). The mean body mass index (BMI) was 29.5 kg/m^2—28.7 for males and 32.3 for females. All patients were informed of the purpose of the double position sensor-study and gave informed consent. The study was classified locally as a technology assessment of an existing procedure without added discomfort or other direct consequences for the patient or procedure. Therefore a formal review by our local medical ethics committee was not performed nor required.

Methods

Polysomnogram recordings were carried out using a digital polygraph system (Embla A10, Broomfield, CO, 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 monitored by straps containing piezoelectric transducers. Snoring was recorded through a piezo snoring sensor.

Determination of Body and Head Position during Sleep

Two position sensors (Sleepsense, St. Charles, IL, USA) were used to determine the position of the trunk and head. The first was placed at the lower part of the sternum, the second in the middle of the forehead just above the eyebrows. The sensors generated 5 discrete output voltage levels corresponding to the following sleep positions: upright, supine, prone, left, and right, with a threshold angle of ± 10 degrees from the 45-degree position boundary. The output of the 2 different position sensors was recorded simultaneously on 2 separate channels of the recording device. In making inferences about body position, it is crucial that the position sensor data truly reflect the actual position of trunk and head in the patients. This was assured at different levels: first, the position sensor readout should reliably reflect the orientation of the sensor relative to the direction of gravity. This was checked with regular intervals in a calibration setup and also during patient preparation by moving the subjects in different positions. Subjects were also requested to keep the upper part of the bed horizontal and were asked to sleep with just a single pillow. Secondly, to accurately reflect body posture, the sensors should be secured firmly to relatively rigid parts of the trunk and head. Therefore, sensors were taped directly to the skin with self-adhesive tape on locations where under normal circumstances, with the subject lying supine, the surface is horizontal. Also, the median forehead and the lower part of the sternum are locations with the least possible amount of subcutaneous tissue. This minimizes possible movement of the sensor relative to the rigid underlying structures of the trunk and skull. The position sensor is quite flat, so there is little chance for a rotation of the sensor relative to the underlying body surface. In all subjects it was verified the following morning that the position sensors were not dislocated. In case of dislocation, subjects were excluded from further analysis in this study. In a total of 50 subjects (approximately 20 of whom were included in this study, the exact number was not recorded at the time) it was verified by overnight video-surveillance that the position sensor data corresponded well with visually observed positions. Finally, sensor characteristics should remain stable throughout the night. Well known are slow drifts in the output of devices based on acceleration sensors. The sensor we employed is an electromechanical type, mainly based on the displacement of a small mercury droplet within the sensor in different positions. The output consists of 5 clearly separated voltage levels corresponding to those different positions. These voltage levels are digitized by the polysomnographic device and stored in a raw data file on the computer as a sequence of numbers. Numerical analysis of these data files demonstrated a good reproducibility, and did not show significant overnight drifts or possibly confounding spurious sensor output signals.

Data Analysis

All signals were analyzed offline on a PC according to the default settings of the polygraph software (Somnologica, Broomfield, CO, USA). Automated results were verified by visual inspection of the entire hypnogram and if necessary corrected if distorted (by artifacts). Sleep stages were scored according to the standard criteria of Rechtschaffen and Kales on 30-sec epochs.[7] Respiratory events were scored according to the AASM 2007 criteria.[8] Apnea was defined as an episode of ≥90% oronasal airflow reduction for ≥10 sec. Hypopnea was defined as an episode of >30% reduced oronasal airflow for ≥10 sec accompanied by a decrease ≥4% of the arterial oxyhemoglobin

saturation. The apnea hypopnea index (AHI) was calculated as the combined number of apnea and hypopnea episodes per hour sleep.

Despite the possibility of simultaneous recording of 2 position channels, the standard software system does not allow analysis of multiple position data channels at the same time. Therefore, 2 overnight hypnograms were constructed: one employed the data from the trunk position sensor, the other employed the data from the head position sensor. All other hypnographic data channels and parameters were the same. From both these hypnograms, the overnight AHI in different positions was determined.

To investigate the effect of trunk and head position on the AHI we employed a multi-step approach: first, we identified subjects with OSAS (AHI >5) from our study population. Secondly, OSAS patients who spent >5% and <95% of the total sleeping time in supine position, based on the trunk position sensor readout, were analyzed for position dependence. Position dependence was defined as an overnight AHI in supine position (determined for both the trunk position sensor and the head position sensor) at least twice as high as AHI in non-supine positions.{Cartwright, 1991 #25}[1,3] Since we used 2 position sensors, this led to 4 possible classifications: both trunk and head supine dependent; only trunk supine dependent; only head supine dependent; and not supine dependent. Thirdly, to evaluate the importance of the head position relative to the trunk position, we further analyzed all subjects with trunk supine position dependence. If the overnight AHI in head supine position exceeded the AHI in trunk supine position by ≥5, the patient was classified as having head position-aggravated trunk supine position dependence. If the overnight AHI in head supine position proves to be higher than in trunk supine position, this would support our initial hypothesis that in some patients the clustering of respiratory events is related more to head position than to trunk position. The dichotomy between subjects based on an AHI difference ≥5 between positions is in itself not sufficient to clarify the clinical importance of the head position. The relatively low cutoff value serves mainly to separate subjects in whom there is no difference between head and trunk position, or a difference possibly caused merely by chance. In the remaining group with a possible clinically significant head position-aggravated trunk supine position dependence, we can further evaluate the quantitative aspects of the interaction between the position of the head and trunk in more detail. Therefore, finally, we combined the data from both position sensors to determine the AHI over 4 possible situations: 1 – trunk supine + head supine; 2 – trunk supine + head not supine; 3 – trunk not supine + head supine; 4 – trunk not supine + head not supine. Our standard software did not allow for this distinction to be made. Therefore we developed custom software to recode the position data of the 2 sensors into the 4 position classifications given above. In subjects with head position-aggravated trunk supine position dependence, we reanalyzed the data to examine the interplay between head and trunk position and the respiratory events. This final reanalysis was performed retrospectively in a later phase of the preparation of this manuscript, on previously archived data. Only the new combined position classifications were entered in the reanalysis. Previously scored hypnograms, i.e., sleep stages and detection of respiratory events, were retained from the archived data.

Statistics

Data were analyzed using Excel 2003 (Microsoft, Redmond, WA) and the SPSS statistical package (version 16-18, SPSS Inc, Chicago, IL). Differences between head and trunk position based results were analyzed using the Student *t*-test. Polysomnographic data often show a non-strictly normal distribution. However, the Student *t*-test is considered quite robust to slight deviations of normality. Additional tests were performed using nonparametric statistics (Wilcoxon/ Mann-Whitney). These yielded essentially similar results and are not displayed. Numerical relations between variables were evaluated through linear correlation.

RESULTS

Of the 300 subjects, 241 were diagnosed with OSAS based on an AHI >5. Of these 241 patients, 42 were excluded from further evaluation. Twenty were excluded because of technically insufficient data, mostly due to excess of artifacts or sensor dislocation. Twenty-two patients were excluded because they spent >95% (n = 10) or <5% of the total sleep time (n = 12) in supine position. The data from the remaining 199 patients were further analyzed for position dependence. In 82 patients (41.2%), the overnight AHI was not position dependent. One hundred four patients (52.3%) were found to be trunk supine position dependent. Of these 104 patients, 102 were both trunk and head supine position dependent. Thirteen patients (6.5%) were not position dependent based on the position sensor on the trunk and were classified as only head supine position dependent. In the trunk supine position dependent group (104 patients), head position was of considerable influence on the AHI in 48 (46.2%) patients. These met the criteria for a head position-aggravated trunk supine position-dependent OSAS. These results are depicted graphically in the flowchart (Figure 1) and conform to the STARD guidelines.[9]

Figure 2 shows the hypnogram in one individual in whom the AHI in trunk supine position (21.4/h, sleeping in trunk supine position 79.9% of the total sleeping time) is almost the same as the AHI calculated over the total sleeping time (23.6). Based on our predefined criteria, this patient does not have a supine position-dependent OSAS (AHI not in trunk supine position = 30.8). However, the overnight AHI in head supine position is much higher (76.8, during 16.6% of the total sleeping time), indicating a head supine position-dependent OSAS. The clustering of apnea in this patient is clearly more related to supine position of the head than to trunk position (no evidence was found suggesting dislocation or malfunction of the position sensors). A general picture was seen in the majority of head supine position-dependent subjects but not trunk supine position-dependent OSAS subjects (n = 13) with visual analysis of the hypnograms. These subjects slept a relatively long proportion of total sleep time in trunk supine position. During the largest part of sleep in trunk supine position, the head was turned sideways. Respiratory events clustered during only a small part of the time spent in trunk supine position. Because of this, these patients did not meet our predefined criteria for a trunk supine position dependent OSAS.

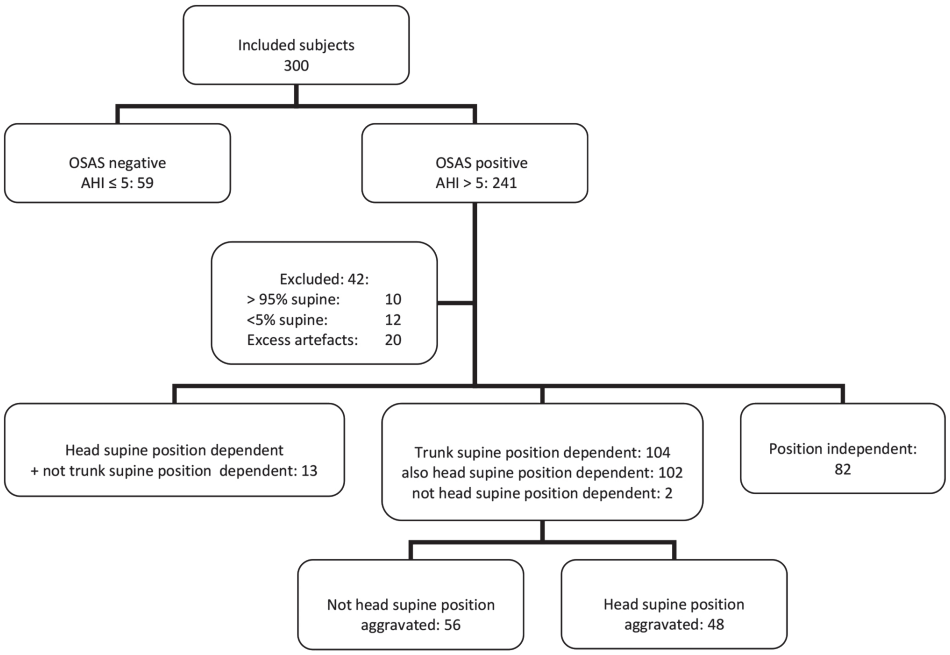

Figure 1 - Flowchart of subjects included in the study.

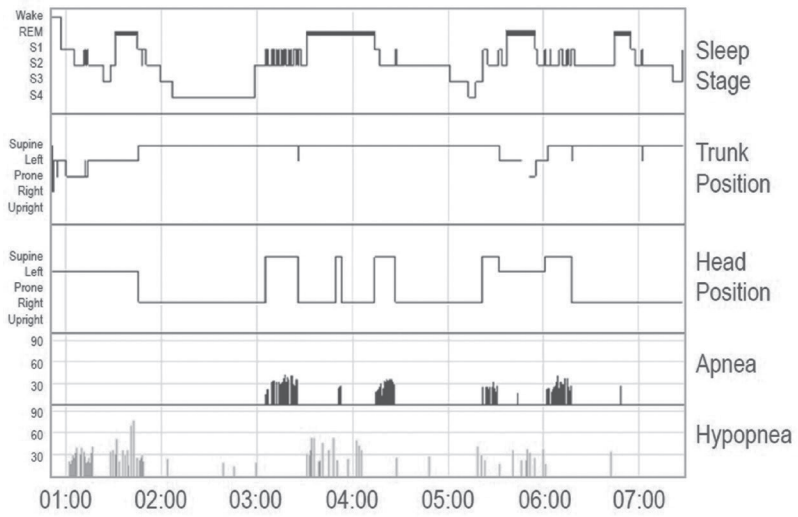

Figure 2 - Overnight hypnogram in a single subject with respiratory events and trunk/head position indicated. Normally, there is only a single position channel displayed. To show the effect of head position, the head position channel recording was inserted into the standard hypnogram report by means of a picture editor program. Notice that in this subject apneas are primarily related to the position of the head, not to the position of the trunk. Hypopneas are more apparent in the remainder of the night.

Table 1 summarizes the demographic and polysomnographic characteristics of the 199 patients diagnosed with OSAS. In our inclusion criteria we made no distinction between men and women. The men outnumbered the women in a proportion similar to that in our general OSAS population. The proportion of women in the head position-aggravated trunk supine position-dependent group (10/48) did not differ significantly from the proportion of women in the total OSAS group (38/199, $\chi 2$ test). Although the average BMI in women was higher than in men and women spent more time in supine position, position dependence of the overnight AHI was more pronounced in men. The average AHI in trunk supine position in the OSAS positive subjects was higher than the average AHI during total sleep time. Also, the average overnight AHI over the entire group was higher in head supine position than in trunk supine position.

Table 1 – Demographic and polysomnographic characteristics* of OSAS-positive-patients (average [±SD]).

Characteristic	Male	Female	Total
Patients (n)	161	38	199
Age (years)	47.7 (10.5)	49.4 (13.6)	48.0 (11.1)
BMI (kg/m2) #	28.7 (4.6)	23.4 (18.8)	27.6 (20.9)
AHI (events/h)			
Total	28.6 (21.3)	23.4 (18.8)	27.6 (20.9)
Trunk supine #	40.1 (24.0)	25.6 (19.8)	37.3 (23.9)
Head supine #	44.9 (26.9)	33.3 (26.5)	42.7 (27.1)
% time in *tsp* #	44.2 (20.7)	53.3 (22.9)	45.9 (21.4)
% time in *hsp*	31.6 (20.4)	31.1 (24.2)	31.5 (21.1)
AHI *hsp* minus AHI *tsp*	4.8 (16.8)	7.7 (13.7)	5.3 (16.2)
AHI *hsp* / AHI *tsp* ratio (%)	131 (106)	134 (93)	132 (103)

* BMI = body mass index, AHI = apnea hypopnea index, OSAS = obstructive sleep apnea syndrome, SD = standard deviation, *hsp (head supine position), tsp (trunk supine position)* = values in supine position based on head and trunk position sensor respectively.
# indicates statistically significant difference for males and females (*t*-test and Mann-Whitney: $P < 0.05$).

Figure 3 graphically summarizes the AHI values determined over the different time periods in OSAS subjects (n = 199). The average AHI over the entire night was 28 (SD 21, median 21). In the trunk supine position, this was 37 (SD 24, median 32). The average AHI in supine position based on the head position sensor was 43 (SD 27, median 41). The differences between the 3 different AHI values are all significant at the level of $P < 0.001$ with both parametric and nonparametric statistics (paired Student t- and Wilcoxon signed rank test).

Figure 4 shows the correlation of the AHI determined over the total sleep time with the AHI during trunk-supine position for the entire OSAS positive study population (n = 199). Observe the extensive spread of the points lying above the unity line (x = y), indicating a higher AHI in trunk supine position in a considerable proportion of subjects. This is in line with previous findings in literature on position dependent OSAS.

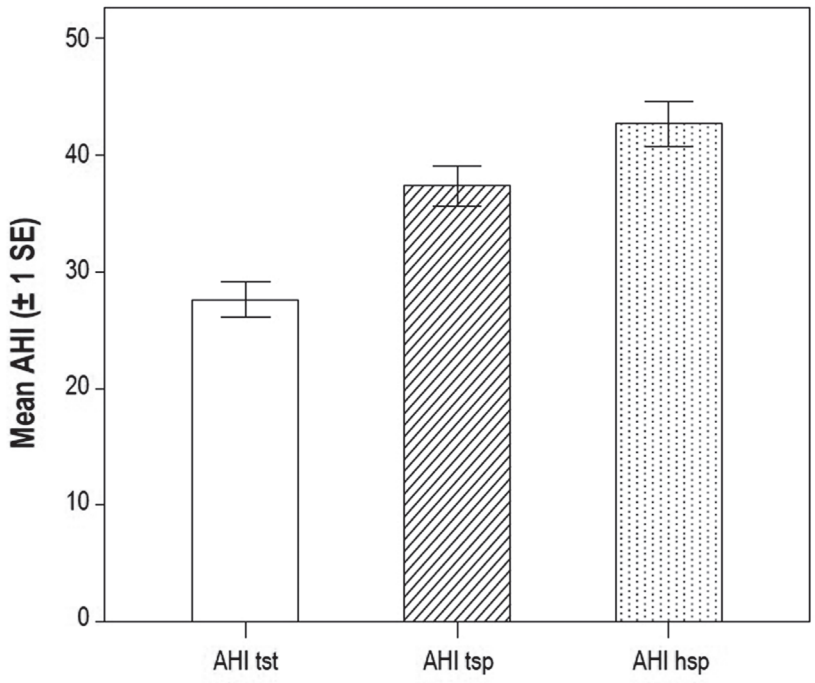

Figure 3 - Mean AHI values determined over the total sleep time (TST) and the different time periods spent in supine position based on the trunk position sensor (tsp) and head position sensor (hsp) in OSAS patients (n = 199).

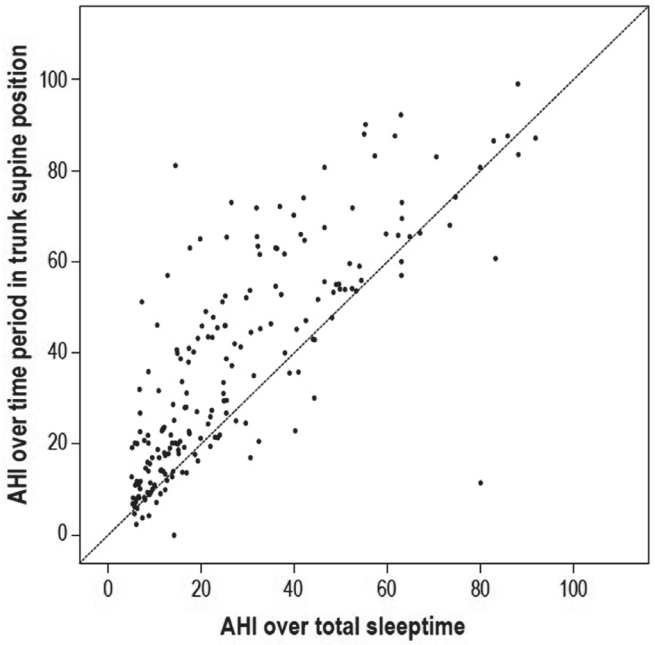

Figure 4 - Correlation of the AHI determined over the total sleeping time with the AHI during trunk-supine position for OSAS positive subjects (n = 199, using the standard trunk position sensor). The line indicates the unity line (x=y).

Figure 5 shows that there is a clear correlation between the overnight supine AHI based on the trunk and head position sensor (r^2 = 0.65). Most points fall on the unity line, indicating an equal AHI with trunk and head supine position. However, again there are a marked number of outliers, mainly above the unity line. This is reflected in the trajectory of the linear regression line. (The straight line in the graph indicates the linear regression line. The unity line is not drawn, but clearly visible by the clustering of points on the x = y line.) The figure illustrates that the higher average AHI in head supine position is not a structurally present factor in all subjects but only seen in a subgroup of subjects. Thus, the effect of position on the AHI may be undervalued based on the AHI in trunk supine position. A number of subjects, with various trunk supine position AHI values demonstrated a head supine position AHI of zero. On review, these were patients in whom the head was always turned sideways while sleeping on the back.

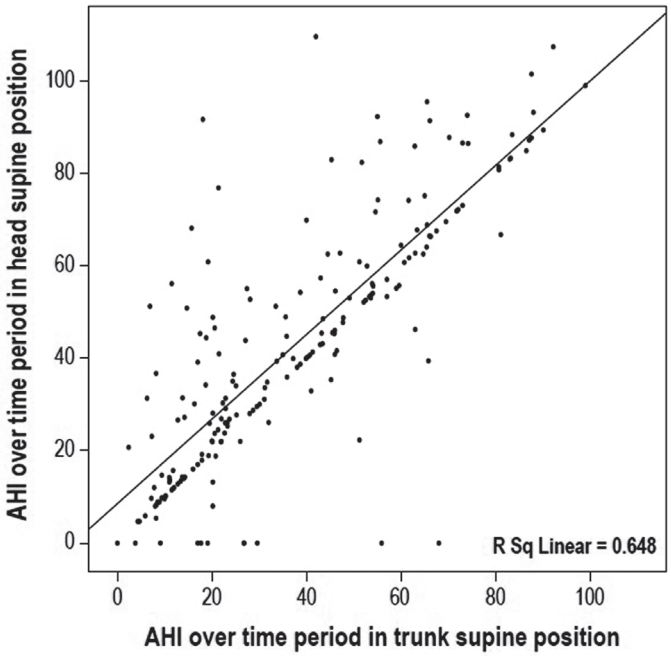

Figure 5 - Correlation of the AHI over the time period spent in supine position based on the trunk position sensor (x-axis) and head position sensor (y-axis). The line indicates the linear regression line of the correlation between the 2 AHI values in our OSAS positive study group (n = 199).

Figure 6 shows the correlation between the relative time spent in different positions. The average duration of trunk supine position was 46% of total sleep time (SD 21, median 46%). It is apparent that in the majority of subjects, trunk supine position time was equal to head supine position time (while lying on the back, the head was also in the supine position). However, in a considerable number of subjects, head supine position time was shorter than trunk supine position time. This indicates that during part of the time spent in the trunk supine position, the head was turned sideways.

On average, the duration of the time spent in head supine position was 77% of trunk supine position time. In a few subjects, head supine position time was longer than trunk supine position time. This suggests that these subjects were sleeping with the trunk slightly turned sideways while the head remained in the supine position.

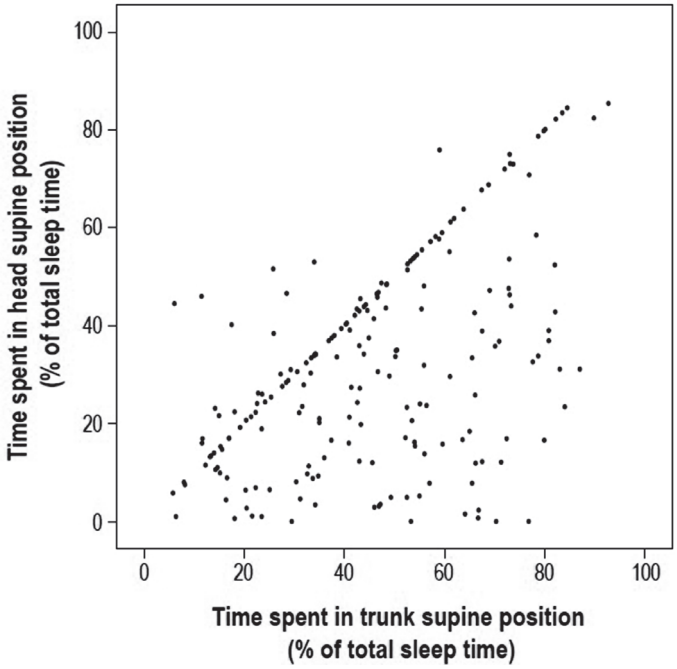

Figure 6 - Correlation between the relative time spent in supine position based on the trunk and head sensor in OSAS positive subjects (n = 199).

In subjects with a head position-aggravated trunk supine position-dependent OSAS, we additionally examined the interaction between head and trunk position and the effect this had on the AHI. The stored data for one subject could not be fully recovered due to a storage failure. Therefore data from 47 subjects were available for analysis (37 male, 10 female).

Figure 7 shows the relative time spent in the different positions of head and trunk for men and women. Three conclusions can be drawn based on these graphs. First, approximately, on average, half of the total sleep time in this subgroup was spent in trunk supine position. Secondly, in more than half of the time spent in trunk supine position the head was turned sideways. Thirdly, the percentage of time spent in trunk supine position was somewhat higher for women than for men.

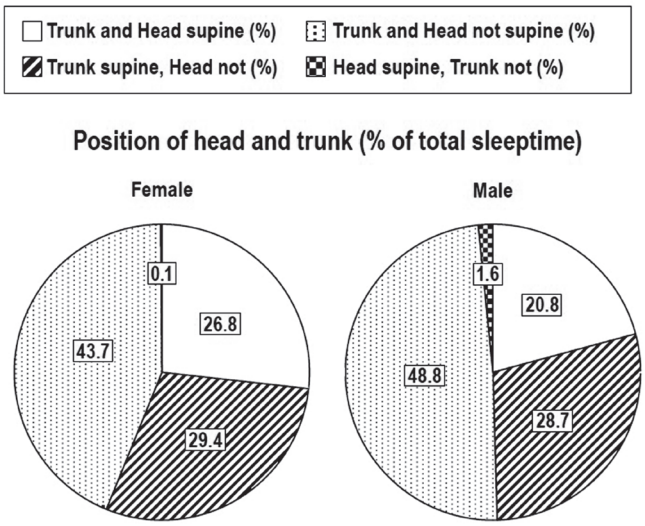

Figure 7 - Relative time spent in the different positions of head and trunk for men and women in patients with head position-aggravated trunk supine position-dependent OSAS (n = 47).

Figure 8 displays the AHI calculated over the time spent in the different positions. The AHI was highest over the time period in which both trunk and head were in supine position. There is a significant difference between this value and the AHI over the time period spent in other positions (paired Student t-test, $P < 0.001$) for both men and women. The effect of sideways rotation of the head when lying in trunk supine position was larger for men than for women (men: mean AHI 65 > 17, difference = 48; female: mean AHI 52 > 15, difference = 37, Student t-test, $P < 0.001$).

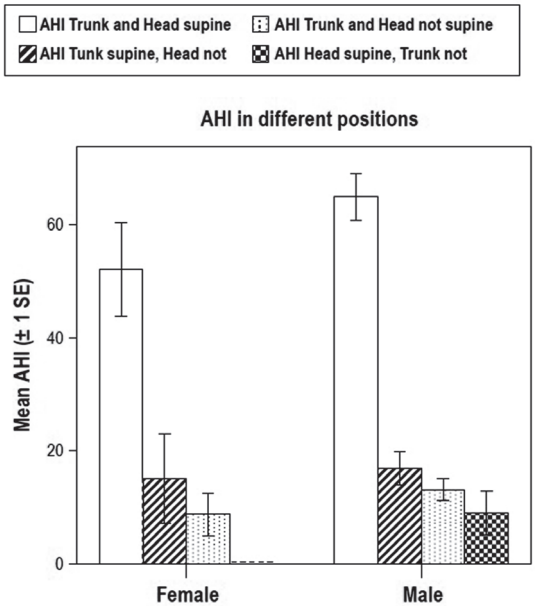

Figure 8 - Mean AHI over the time spent in the different positions of head and trunk in patients with a head position-aggravated trunk supine position-dependent OSAS (n = 47).

DISCUSSION

The results from this study confirm our hypothesis that head position, separately from trunk position, is an additional important factor in the occurrence of apnea/ hypopnea in a subpopulation of OSAS patients. Unfortunately, routine PSG is most often limited to recording of trunk position solely. While preparing this study we were confronted with the apparent lack of standardization of position recording during sleep studies. Our results indicate that these technical factors deserve more attention in the development of future clinical standards.

Overnight results based on the two different sensor positions show that the AHI calculated over the total sleep period with the head lying supine frequently was higher than the AHI calculated over the total period with the trunk in supine position. This occurred in a considerable proportion of OSAS subjects (48 head position-aggravated trunk supine-position dependent + 13 solely head supine position dependent out of 199 = 30.7%). In the patients with an overnight head position-aggravated trunk supine position-dependent OSAS (n = 48), the effect of head rotation was further confirmed. Over the time period when lying on the back with the head also supine, the AHI was significantly higher than during the time period with the head turned sideways.

Overnight position dependence was defined as an AHI in supine position at least twice as high as the AHI in the other positions. The same definition has been used in previous studies.[1,3] As with every cutoff value, this distinction is somewhat arbitrary. However, with this criterion, we think we select only those subjects in whom there is a relevant (and likely etiological) difference between supine position and other positions. Head position dependence was defined as an AHI difference of 5 or more between head and trunk position recordings. This low threshold was chosen to select subjects with a possible clinically relevant head position dependence for further analysis. If we would use a higher cutoff value we would have increased the clinical relevance of the distinction. However, we would also introduce a larger selection bias which would hamper further quantitative analysis and interpretation of the results in this subgroup.

For the detection of rotation, we used the same sensor as commonly is used for detection of trunk rotation in many commercially available systems. The use of a sensor with a threshold for rotation detection of 45 degrees could lead to an underestimation of rotation of the head when this is only a slight rotation. Review of the data and our previous observations indicate that in the majority of subjects there are frequent head turns which exceed this 45-degree detection threshold. We rarely saw quick fluctuations in position sensor readout, which would indicate a rotation in an angle around the detection threshold. The 45-degree threshold seems also justified because smaller rotations would have less pronounced mechanical effects on the anatomical configuration of the upper airway. Although this study was not aimed at unravelling this underlying pathophysiological basis, a change in the local anatomical configuration of the upper airway during head rotation seems a likely underlying factor. With the head in supine position, the tongue and to a lesser extent the soft palate, in accordance with gravity, fall backward due to the physiological muscle relaxation. In the trunk supine position with the head turned to either the left or right side, this effect of gravity on the tongue and soft palate would presumably be smaller, causing fewer obstructive events in the upper airway. Another possibility is that rotation of the head exerts a stretching force on the wall of the upper airway, which decreases the susceptibility to airway collapse during sleep.

We mainly focused our investigation on the effect of lateral rotation of the head. Of course, flexion and extension of the neck could have a similar effect on the AHI. However, with the patient lying on a horizontal bed with the head supported by a single pillow, movement freedom to flexion and extension is more limited than lateral rotation. If lateral rotation was associated with flexion of the neck, one would expect an increase of the AHI with sideways rotation due to increased mechanical compression. On the contrary, the AHI decreases with lateral rotation in a subgroup of patients. Lateral rotation associated with hyperextension of the neck could possibly reduce the tendency for airway collapse. However, during video-surveillance in our center, we rarely observed either major flexion or extension movements of the head during sleep that could have a distinct influence on respiratory events. Flexion-extension of more than 45 degrees would also be detected by the head position sensor. This almost never occurred in our study population. Small flexion and extension movements could potentially already have a major effect on the anatomical configuration of the upper airway, and as such affect the AHI. However, if this was relevant, small flexion-extension movements should cause major fluctuations in flow and clustering of apneas in time periods over which the recorded position of the head (and sleep stage) remained constant. This was not observed in our data. Clustering of apneas seemed primarily related to the recorded supine position of the head, with an overall reduction of apneas during recorded lateral rotation. Thus, although we cannot disprove conclusively that head flexion-extension may partly explain our results, we believe this is less likely, but further research is needed to rule out or support this possibility more specifically.

Looking at the demographic characteristics there are some clear gender differences. In the present study, position dependence of the AHI for both trunk and head supine position was more pronounced in men, despite the fact that women had a higher average BMI and spent more time in supine position.

We did not investigate the relation between AHI parameters based on trunk and head position and the different sleep stages. Respiratory events are known to be more prevalent in sleep stage 2 and in REM sleep. Sleep architecture is heavily influenced by the severity of OSAS. One could, for example, hypothesize that head supine position is more often associated with REM sleep or sleep stage 2. However, visual review of the hypnograms in our study group gives no support for this hypothesis. Full quantitative analysis of the interaction between sleep stages, position, and respiratory events would require a more elaborate study design, possibly in a larger patient cohort.

The data reported here are not only interesting from a scientific point of view; they have clinical relevance as well. Two recent studies on the role of sleep position have shown a remarkably consistent 56% of OSAS to be position dependent (defined as having a AHI at least twice as high in a certain sleep position than in another position).[1,6] The worst position is usually supine, but not always. Another 30% of patients do worse in a certain (usually supine) position but not with an AHI twice as high as in another position. So in roughly 80% of patients, sleep position is reported to play an important role in the severity of OSAS. Note that results in literature all seem based on recording the trunk position. Our results indicate that trunk position-based data may underestimate the effects of position on respiratory events.

The percentage of sleeping in the worst sleeping position may very well be the most important factor in night to night variability in sleep studies.[10,11] Given these facts, it is remarkable that in sleep studies, both primary as well as in reporting results of therapeutic interventions (surgery, oral appliance therapy, etc.), the severity of the OSAS and the percentage of sleeping time in the various positions is not routinely reported. For a meticulous reporting of interventions, ideally the severity and the amount of sleeping in different positions should be reported as well.

Apart from diagnostic accuracy, our results may also have therapeutic consequences, both in surgical and nonsurgical strategies. For example, position therapy of OSAS now commonly aims to arouse the patient when lying on the back so the subject rotates the body on his/ her side to alleviate respiratory obstructions.[12,13] In head position-aggravated trunk supine position-dependent OSAS, it may be sufficient to stimulate the subject to rotate only the head sideways, based on a position sensor monitoring the orientation of the head. It can be expected that this would have a much less profound negative effect on sleep quality.

In conclusion: We have provided evidence that in a significant proportion of patients, trunk and head position during sleep are not the same. In addition, this may have clinical relevance. OSAS is almost per definition caused by obstruction in the upper airway, and it makes sense to analyze head position in addition to trunk position. This study warrants further research in the underlying pathophysiological and clinical consequences.

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CHAPTER 2

The undervalued potential of positional therapy in position dependent snoring and obstructive sleep apnea – a review of the literature

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ABSTRACT

Study objective

Research during the past 10 -20 years shows that positional therapy (PT) has a significant influence on apnea hypopnea index. These studies are predominantly performed as case series on a comparably small number of patients. Still, results have not found their way into the daily diagnostic and treatment routine. An average 56% of patients with obstructive sleep apnea (OSAS) have position dependent OSAS (POSAS) commonly defined as a difference of 50% or more in apnea index between supine and non-supine positions. A great deal could be gained in treating patients with POSAS with PT. The aim of this paper was to perform a thorough review of the literature on positional sleep apnea and its therapy.

Methods

A broad search strategy was run electronically in the MEDLINE and EMBASE database using synonyms for position and sleep apnea.

Results

Sixteen studies were found which examined the effect of positional therapy on OSAS. In this literature review we discuss the various techniques, results and compliance rates.

Conclusion

Long-term compliance for PT remains an issue, and although remarkable results have been shown using innovative treatment concepts for PT, there is room for both technical improvement of the devices and for further research.

INTRODUCTION

Snoring and obstructive sleep apnea syndrome (OSAS) are the most prevalent sleep-disordered breathing problems. OSAS affects 2 - 26% of the general population, depending on gender, age, and definition of the used criteria.[1,2] OSAS is associated with significant morbidity, such as excessive daytime sleepiness, social unacceptable snoring and impaired quality of life. Patients are at higher risk of developing cardiovascular diseases.[3,4] If the apnea hypopnea index (AHI) is > 40 the risk of being involved in a traffic accident increases.[5,6]

Adequate treatment is of key importance. Continuous positive airway pressure (CPAP) is regarded as gold standard treatment of OSAS, with mandibular advancement device (MAD) therapy or surgery in reserve for CPAP failures.[7] Unfortunately, 29 -83% of patients prescribed CPAP are non-adherent and use their CPAP less than 4 h per night.[8,9] In cases of CPAP failure treatment remains indicated. MADs and a variety of surgical interventions are then available.[10-15] All these treatment modalities have their specific downsides.

Conservative treatment of OSAS can be just as crucial: lifestyle alterations such as weight reduction, abstinence of alcohol and sedatives and avoidance of supine sleeping position, where appropriate. Significant improvement and even remission was recorded in obese patients diagnosed with OSAS undergoing bariatric surgery (BS).[16] The latter should be considered as a treatment option for patients with severe OSAS and obesity alongside CPAP.

A number of papers have been published on the role of supine position on OSAS and methods to avoid supine position. In 1948, in a “plea for more serious consideration of snoring”, Robin states that “sleeping on one’s back is considered a common cause of snoring”.[17] It is likely that spouses of (apneic or non-apneic) snorers were the first to identify the role of body position on the severity of the snoring or apnea of their bed partner. In 1984 Chest published a letter written by a patient’s wife.[18] She had cured her husband’s sleep apnea snoring problem by “having sewn a pocket into the back of a T-shirt and having inserted a hollow, lightweight plastic ball, to prevent her husband sleeping on his back”. During the American War of Independence (1775 - 1783) and later during World War I (1914 - 1918), soldiers were advised to wear their rucksacks (filled with a bulky mass) whilst sleeping, in order to avoid sleeping on their backs and reduce snoring, as to avoid making their position known to the enemy.

PT, in whichever form, has been found to have a significant influence on snoring and OSAS severity.[7] Still, results have not found their way into the daily OSAS diagnostic and treatment routine, even though approximately 56% of patients with OSAS have position dependent OSAS.[19-22] Why is PT unfashionable?

By means of a thorough review of the literature on positional sleep apnea and its therapy, this study aims to provide an overview of the various PT techniques and their success and compliance rates.

METHODS

A broad search strategy was run electronically in the MEDLINE and EMBASE database on the 5th of October 2011 by one researcher (M.R.): ("Position" OR "position dependent" OR "positional" OR "posture") AND ("apnea" OR "apnoea" OR "OSA" OR "OSAS" OR snor*). In addition, the reference lists of included articles were screened for additional relevant citations. Studies were evaluated according to the Oxford Centre for Evidence-based Medicine levels of evidence (Table 1).

Table 1 - Oxford Centre for Evidence-based Medicine levels of evidence.

Level	Therapy
1a	Systematic review of randomized controlled trials
1b	Individual randomized controlled trial
2a	Systematic review of cohort studies
2b	Individual cohort study
2c	"Outcomes research"
3a	Systematic review of case-control studies
3b	Individual case-control study
4	Case series (with or without comparison)
5	Expert opinion

Diagnosis

Current definition of OSAS, positional obstructive sleep apnea (POSAS)

The recommended objective diagnostic criteria for OSAS include an AHI of 5 or more and evidence of daytime sleepiness. The AHI is defined as the mean number of apneas and hypopneas per hour during sleep, an apnea is a period of 10 s or more with a reduction of oronasal airflow of > 90 %. A hypopnea is defined as 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.[23, 24]

Cartwright was the first to describe the arbitrary cut-off point of a *difference of 50% or more in apnea index between supine and non-supine positions*.[25] This is the most common definition for positional obstructive sleep apnea (POSAS) used today, but many question Cartwright's criteria and apply adapted versions.

Both Mador's and Permut's group defined POSAS as follows: "an AHI of fewer than 5 events per hour while in the non-supine position as well as a decrease in the AHI by more than 50%".[26, 27] In 1998 Marklund *et al* defined supine-dependent sleep apnea as follows: a supine AHI ≥ 10, together with a lateral AHI < 10.[28] In the study of Bignold *et al*, when patients met the following criteria, they were deemed position dependent: "overall AHI ≥ 15/h, supine AHI ≥ twice the non-supine AHI; ≥ 20 minutes of sleep in supine and non-supine postures and non-supine AHI < 15".[29]

Sleep study with sleep position assessment and separate assessment for head and trunk

Sleep studies exist in many varieties, from very simple to very detailed. In order to determine if a patient is position-dependent, it is clear that assessment of the sleep position is mandatory. In every OSAS patient, the role of sleep position should be investigated. The role of sleep studies without sleep positional recording is therefore very limited. Ideally, both the mean AHI as well as the separate AHIs in supine, left, right and prone sleep position should be recorded. In the hypnogram, this is reflected by a clustering of respiratory events correlated with the change in body position.

Commonly, position sensors are attached to the elastic bands around either the chest or abdomen. Our group recently confirmed the hypothesis that the occurrence of OSAS may also be dependent on the position of the head.[30] Study subjects underwent overnight polysomnography with two position sensors: one on the trunk, and one in the mid-forehead. Overnight results based on the two different sensor positions show that the AHI calculated over the total sleep period with the head lying supine was frequently higher than the AHI calculated over the total period with the trunk in supine position. Over the time period when lying on the back with the head also supine, the AHI was significantly higher than during the time period with the head turned sideways. The use of dual position sensors could have major clinical and research implications.[31] In patients with a suspicion of position-dependent OSAS, sleep recording with dual position sensors placed on both trunk and head should be considered.

Prevalence of position dependent OSAS and snoring

A considerable amount of literature exists on the role of sleep position in OSAS.[19-22, 25, 26, 30-37] In studies from Israel and the Netherlands a remarkable steady 56% of patients with OSAS have a difference of 50% or more in apnea index between supine and non-supine positions.[19-22] An additional 30% of patients have a higher AHI in supine position than in the other positions, but not twice as high. On average patients with POSAS have a lower BMI and are younger than non-positional OSAS patients.[19, 22]

Reports have suggested that snoring is aggravated by a supine sleeping position.[25, 28] Nakano *et al* described the effect of position on snoring in 21 non-apneic (AHI <15) and 51 apneic patients (AHI > 15).[39] They conclude that "snoring time as well as snoring intensity was lower in the lateral position than in the supine position in the non-apneic patients whilst in the apneic group neither snoring time nor intensity had statistical differences". In non-apneic patients the snoring time was 17.5% and 6.4%, the intensity 101.6 and 98.3 dB in the supine and non-supine position respectively. In the apneic group, the snoring time was 16.9% and 15.4%, the intensity 102.9 and 103.5 dB in the supine and non-supine positions, respectively.

Choi *et al* defined a position-dependent snorer as "one who has a greater than 50% reduction of snoring rate in the lateral position compared to that in the supine position".[40] To our best knowledge the prevalence of position dependent snoring is yet to be reported.

Positional therapy

PT 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.[35] Various techniques are described to prevent patients from assuming the supine position such as positional alarms, verbal instructions, tennis balls (TBT), vests, "shark fins" or special pillows.[7, 27, 29, 40-53]

The effect of positional therapy on snoring

Rationale

In 1948 Robin, stated that "many persons snore only when on their backs" and suggests that on some occasions sewing a cotton reel sewn into the back of a pyjama can be effective albeit rather uncomfortable.[17] The effect of PT on snoring can be measured from various angles: intensity (decibels), frequency (snores/hour), snoring rate (% TST) or duration (seconds or milliseconds).

Overview of evidence

Two studies specifically studied the effect of PT on snoring. In five studies evaluating the effect of PT on POSAS, the result on snoring was also mentioned.

Braver and Block reported that PT (foam rubber wedges both behind and in front of subject) was not effective in reducing snoring in 20 patients.[54] The number of snores remained 356/hour both with and without PT.

Choi *et al* evaluated the efficacy of PT (vest with 2 inflatable chambers) to treat snoring in 17 positional dependent snorers, defined as one who has a greater than 50% reduction of snoring rate in the lateral position compared to that in the supine position.[40] The snoring rate decreased from 36.7% to 15.7% without subjective or objective adverse effects.

Maurer *et al* found an overall decrease in snoring time from 180 to 110 minutes in 12 apneic patients treated with PT (vest with semi-rigid foam in its dorsal part), but an increase was observed in 30% of the patients.[41] A statistically significant decrease in snoring was reported by Zuberi *et al* in 22 patients with POSAS treated with PT (triangular pillow), whilst Wenzel *et al* reported a decrease in snoring rate from 15.4% to 9.8% in 14 patients with POSAS treated with PT (vest).[42, 43] Loord and Hultcrantz reported that half of the patients (n = 18) treated with PT (soft vest attached to a board with pillow), snored more frequently, specifically six snored less frequently, nine snored more frequently and for two, there was no difference.[44] A recent study by Bignold *et al* reporting on the efficacy of the position monitoring and supine alarm device on 15 patients with supine-dependent OSAS found no improvement in snoring.[29] There was a trend for an overall reduction in snoring frequency, but this was not statistically significant. Furthermore, there was no difference in mean snore duration.

Conclusion

In non-apneic patients snoring decreased when a patient adopted a non-supine position. In apneic patients, in the majority of studies, PT does not result in an improvement in snoring.

The effect of Positional therapy on OSAS

Overview of the evidence

A number of studies have examined the effect of PT on OSAS.[7] Of the 23 relevant articles found, seven studies were excluded from the overview. Two studies did not provide information on the effect of PT on OSAS parameters and were omitted from the overview.[46, 47] Five studies evaluated the effect on OSAS of an array of devices resulting in an elevated posture and head extension.[55-59] As these devices did not prevent the patient from assuming the supine position we did not include these studies in our review. An overview of the 16 included articles is presented in Table 2.

Various techniques are described to prevent patients from assuming the supine position such as an upright sleep posture, positional alarms, verbal instructions, tennis balls, vests, "shark fins" or special pillows.[7, 27, 29, 40-53]

In an attempt to decrease discomfort and improve compliance, our group developed a new treatment concept: a small neck-worn vibrating device, which prevents patients from applying a supine sleeping position.[53] When wearing the device, adopting a supine position, triggers a vibration which increases in intensity until a new position is adopted, without significantly reducing total sleep time or disrupting sleep. Thirty patients with positional sleep apnea were included in a pilot study. No side effects were reported. The mean AHI dropped from 27.7 ± 2.4 to 12.8 ± 2.2. Seven patients developed an overall AHI below 5 when using the device in ON modus. Although the results are encouraging, several items remain to be addressed with this device and there is room for improvement. The long-term effect remains to be studied.

Bignold *et al* evaluated the efficacy of a similar device in 15 patients fulfilling the following criteria: overall AHI ≥ 15/h, supine AHI ≥ twice or greater than the non-supine AHI; ≥ 20 minutes of sleep in supine and non-supine postures and non-supine AHI < 15.[29] Subjects were assigned to receive the active PT or the inactive PT in a random order for a week followed by a 1-week washout before commencing the alternative treatment. The device consists of a position monitoring and supine alarm device fastened to the chest. The mean baseline AHI (24.1) was reduced in the order of 45% with active treatment.

Three publications studied the effect of PT compared to CPAP in a randomized crossover study set-up. Jokic *et al* included 13 patients who were randomized to 2 weeks of treatment with nCPAP or positional therapy (backpack with softball) followed by a cross-over to the other modality.[48] They found "PT to be highly effective in reducing time spent in a supine position". And although both treatment modalities were found to improve OSAS severity, nCPAP was found to be more effective in reducing the AHI (17.9 to 3.4 on nCPAP, to 9.5 with PT).

Skinner *et al* included 20 patients in a randomized cross-over comparing the efficacy of a thoracic anti-supine band (TASB) with nCPAP.[51] Subjects were randomly assigned to receive the TASB or nCPAP for the first month followed by a 1-week washout before commencing the alternative treatment. The baseline AHI was 22.7 and was decreased to 12.0 with TASB and 4.9 with nCPAP.

Table 2 - Overview literature on positional therapy.

Author	Year	Design	LoE	No.	BMI (kg/m²)	PT method	Mean AHI without PT	Mean AHI with PT	Mean TST in supine position without PT (%)
Cartwright[45]	1985	CS	4	10	30.6	PA	54.7	21.4	51.4
Kavey[32]	1985	CS	4	2/4	24.5	TBT	9.2[b,c]	3.8[b,c]	40.4%[c]
Kavey[32]	1985	CS	4	2/4	26.5	Verb Inst	40.8[b,c]	2.8[b,c]	92.1[c]
Cartwright[46]	1991	CS	4	15/60	ND	PA	33.3	20.8	141.1[f]
Cartwright[46]	1991	CS	4	15/60	ND	Verb Inst	26.7	7.7	101.3f
Braver[54]	1994	RcoT	2b	20	36	Foam wedges	17.5	14.1	68
Jokic[48]	1999	RCT	2b	13	30	Backpack with softball	17.9	9.5	25.6
Maurer[41]	2003	CS	4	12	26.5	Vest with semi-rigid foam on dorsal part	26.7	7.6	300[f]
Zuberi[42]	2004	CS	4	22	23-48[a]	Triangular pillow	23.5	11.1	ND
Oksenberg[49]	2006	CS	4	12/78	28.1	TBT	46.5	17.5	79
Wenzel[43]	2007	CS	4	12	28.1	Vest with semi-rigid foam on dorsal part	31.3	13.8	72.2%
Loord[44]	2007	CS	4	18/23	ND	Vest on board with pillow	21.8	14.3	ND
Skinner[51]	2009	RcoT	2b	20	30.7	Thoracic anti-supine band	22.7	12.0	34.4
Permut[27]	2010	RcoT	2b	38	31	Vest with semi-rigid foam on dorsal part	11[d]	2[d]	40[d]
Choi[40]	2011	CS	4	17	ND	Vest with inflatable chambers	7.7	4.8	67.1
Svatikova[52]	2011	RCcoT	2b	18	29	Triangular pillow	39[d]	27[d]	39
Bignold[29]	2011	RcoT	2b	15	28.8	PA	24.1	-[e]	36.4%
van Maanen[53]	2011	RCcoT	2b	30	27.7	Neck-worn vibrating apparatus	27.7	12.8	40

CS=case series, RCT=randomized controlled trial, RcoT=randomized cross over trial, RCcoT=randomized controlled cross over trial, PA=positional alarm, TBT=tennis ball technique, Verb Inst=verbal instructions, AHI=apnea hypopnea index, BMI=body mass index, LoE=Level of Evidence, ND=not described, PT=positional therapy, TST=total sleep time, mo=months, wks=weeks.

[a] Range, [b] AI, [c] Initial diagnosis based on 2 consecutive PSGs. After initial diagnosis, patients studied for an additional one or two nights between four months and 3 years later during which time they avoided sleeping in the supine position, [d] Median, [e] AHI reduction in the order of 45% with active treatment estimated from nasal cannula/oximetry from home-sleep studies, [f] In minutes

Mean TST in supine position with PT (%)	AHI in supine position without PT	AHI in supine position with PT	AHI in non-supine position without PT	AHI in non-supine position with PT	Sleep efficiency without PT (%)	Sleep efficiency with PT (%)	Follow-up
2.1	72.0	11.0	19.3	21.6	ND	ND	-
8.8%[c]	13.7[b,c]	5.1[b,c]	ND	ND	ND	ND	4-12 mo
11.2[c]	42.4[b,c]	6.9[b,c]	ND	ND	ND	ND	3-4 mo
3.4[f]	62.5	32.9	9.7	21.7	ND	ND	8 wks
16.5[f]	87.3	26.8	7.7	4,6	ND	ND	8 wks
ND	ND	ND	ND	ND	ND	ND	-
1.	63.8	ND	4.9	ND	ND	82	-
63[f]	39.3	ND	5.5	ND	81	83	-
ND	ND	ND	ND	ND	ND	ND	-
12.3	57.0	44.4	11.6	13.8	80.9	78.9	2 mo
2.1%	ND	ND	ND	ND	86.3	78.9	-
ND	50.4	ND	ND	ND	ND	ND	3 mo
6.3	59.6	37.8	4.7	10.3	ND	ND	1 mo
0[d]	31[d]	ND	2[d]	ND	89[d]	88[d]	-
25	ND	ND	ND	ND	89.8	87.6	
8	49[d]	51[d]	27[d]	27[d]	ND	ND	-
ND	51.3	ND	9.7	ND	81.4	ND	-
19	59.7	12.5	6.7	11.2	91.9	88.3	-

A successful treatment outcome was defined as an AHI <10, which was achieved in 13 of 18 subjects when using TASB and in 16 of 18 subjects when using nCPAP. Once again they found the self-reported compliance was significantly better with TASB than with nCPAP. 19 of 20 patients reported a 7 hour nightly use of the TASB, whilst only 9/20 patients managed to use their nCPAP at least 4 hours per night.

The recent study by Permut *et al* showed that PT (a bulky mass strapped to the back) was equal to CPAP in normalizing the AHI in patients with a mild to moderate POSAS.[27] Only patients with a non-supine AHI of < 5 were included. The long term effect was not reported.

Conclusion

All studies report a positive effect of PT on the AHI.
PT compliance is better than CPAP compliance, but the latter is a more effective treatment.

Positional therapy compliance

Even the most effective medical devices are only effective, when they are used. Both CPAP and - to a lesser extent - MAD therapy is hampered by compliance issues.[60-62]

Overview of the evidence

Skinner *et al* included 20 patients in a randomized cross-over comparing the efficacy of the thoracic anti-supine band (TASB) with nCPAP.[51] Subjects were randomly assigned to receive the TASB or nCPAP for the first month followed by a 1-week washout before commencing the alternative treatment. The self-reported compliance was significantly better with TASB than with nCPAP. Nineteen of 20 patients reported a 7 hour nightly use with the TASB. In contrast only 9 of 20 subjects met the 4 hour per night CPAP compliance criteria.

Next to the efficacy study of PT (vest with semi-rigid foam on dorsal part) by Wenzel *et al*, the group contacted the patients approximately 13.7 months later by telephone to assess PT compliance.[43] Only 4 of the 14 patients were still using PT (on average for 7.3 hours and 6.4 nights); their ESS was reduced from 8.5 to 6.5. The remaining 10 patients had stopped using PT due to the following reasons: discomfort and tightness of the vest, frequent awakenings, restless sleep, increased sweating during the night and prevention of preferred sleeping position.

Oksenberg *et al* assessed the use of PT (TBT) during a 6-month period in 78 consecutive POSAS patients.[49] Of the 50 patients who returned the questionnaire 38% were still using PT, 24% no longer used PT, as they claimed to have learned to avoid the supine position and 38% no longer used PT but had not learned to avoid the supine position.

Bignold *et al* studied the compliance of 67 patients, who had been prescribed PT (TBT) 2.5 yrs ± 1 yr earlier, using a follow-up questionnaire.[50] 6% were still using PT, 13.4% no longer used PT, as they claimed to have learned to avoid the supine position and a staggering 80.6% no longer used PT, but had not learned to avoid the supine position. Reasons to abort the PT included ineffectiveness, backache, discomfort and no improvement in sleep quality or daytime alertness.

Of the nine patients randomized to PT (triangular pillow), in a study performed by Svatikova *et al*, three months post-stroke, the self-reported adherence was: 3 (33%) all nights, 1 (11%) most nights, 2 (22%) some nights, and 3 (33%) no nights.[52]

In a second study performed by Bignold *et al* patients were assigned with PT for 3 weeks (a position monitoring device and supine alarm device).[29] The device was active for one of the 3 weeks. Patients used the device 85% of nights over the full 3 weeks with an average of 6.8 hours of use per night.

It has been suggested that patients may learn to avoid the supine position following PT and therefore do not need to use PT on a regular basis.[45] Others may need PT either periodically to reinforce training or consistently.

Conclusion

Ineffectiveness, backache, discomfort and no improvement in sleep quality or daytime alertness have been responsible for poor compliance and subsequent disappointing long-term results of PT.

Can the effect of PT be predicted from the sleep study?

Many different forms of sleep study are available, some simple, some more extensive. Some take sleep position into account, others do not. Most provide information on sleep position, time spent per position and the AHI distribution per position. Some PSGs calculate the non-supine AHI; if not the following formula can be used:

$$\frac{\left(AHI_{prone} \times TST_{prone}\right) + \left(AHI_{left} \times TST_{left}\right) + \left(AHI_{right} \times TST_{right}\right)}{TST_{prone} + TST_{left} + TST_{right}}$$

It remains to be studied what the predictive value is of the non-supine AHI. Can it be used to indicate when PT may be successful or to measure the expected effect of PT? Both Mador and Permut's group only included patients with an AHI of fewer than five events per hour while in the non-supine position.[26, 27]

Sleep position and positional therapy in combination with sleep surgery

Rationale

As early as 1948, Robin wrote: "sleeping on one's back is considered a common cause of snoring, as the tongue falls back more readily".[17] He reasoned that "by changing the position of the head the tongue will be prevented from falling back". Harper and Sauerland suggested that "when sleep apnea patients sleep in supine position, the tongue tends to fall backward against the pharyngeal wall, due to gravity".[63] Our group recently reported that visualisation of a base of tongue obstruction or epiglottis obstruction during drug-induced sleep endoscopy (DISE), was more common in patients with POSAS in comparison to patients with OSAS (p = .058).[64]

These results suggest a trend: patients with POSAS may require base of tongue level surgery more often than patients without positional dependence. Is this an overlooked cause of surgery failures?

Overview of the evidence

To our best knowledge 3 papers have been written on the effect of sleep position on treatment outcomes of sleep surgery, the UPPP.

Katsantonis *et al* studied the effect of UPPP on sleep posture and differences in uvulopalatopharyngoplasty (UPPP) results in various sleep positions in a small series of 17 patients.[65] They found that following UPPP, the AHI significantly improved in the lateral position. They also found that during sleep in a supine position, the AHI did not show significant improvement. They conclude that "UPPP enhances the position effect on OSAS because it readily eliminates obstructive events in the lateral sleep position". In other words the difference in AHI in supine and non-supine positions are more pronounced postoperatively. They are of opinion "that additional positional therapy could significantly improve response to treatment with UPPP".

Lee *et al* studied the effect of sleep position on surgical outcomes as well.[66] They studied 69 consecutive patients who underwent a UPPP. After categorizing the patients into four groups according to the change in AHI after surgery, they found that the failure group had a higher proportion of supine position dependency than any other group.

In a second paper published by the same group, results show that UPPP is a successful treatment for obstructive events occurring in the lateral sleep position, especially in patients without positional dependency.[67] The suggestion is made that "patients who have become position dependent may benefit from PT after UPPP".

A Korean study, evaluated the changes of sleep positions before and after pharyngeal (UPPP or uvulopalatal flap or tonsillectomy) and/or nasal surgery (endoscopic sinus surgery and/or septoplasty and/or turbinoplasty) in 52 OSAS patients with no response to surgery (n = 25) and with response to surgery (n = 28).[68] Response was defined as a > 50% decrease in postoperative AHI. They concluded that "the frequency of positional changes was significantly decreased with the improvement of respiratory disturbances and arousals in the response group after surgery".

Conclusion

All three papers conclude that UPPP is most successful in decreasing the AHI in the lateral position. In the supine position, following UPPP, the AHI shows no significant improvement. As the difference in AHI in supine and non-supine positions are more pronounced postoperatively, UPPP enhances the position effect on OSAS; therefore additional PT could significantly improve response to treatment.

Sleep position and positional therapy in combination with an oral device

Overview of the evidence

Four papers were found which studied the treatment outcome of MAD therapy specifically in positional and non-positional OSAS patients.

Cartwright investigated factors associated with the effectiveness of an MAD on OSAS in 16 male patients.[69] Patients with position-dependent OSAS, were more responsive to MAD therapy than

patients with non-position dependent OSAS. The presence of an increased severity of apneas in the supine posture was the strongest predictor of success.

Yoshida studied the effect of an MAD in 72 patients according to sleep position.[70] Forty-four patients exhibited apneas *most frequently* in the supine position, 15 in lateral position, and 13 in prone position. The baseline AHI was significantly lower in the prone group than in the lateral group or the supine group. In the supine group the treatment was successful (defined as an AHI < 10) in 61.4% of the patients, none in the lateral group and 84.6% in the prone group. Yoshida concluded that the effectiveness of an oral appliance is greatly influenced by sleep posture.

Marklund *et al*, in a small series found treatment success to be related to supine-dependent sleep apnea.[28] Supine-dependent sleep apnea was defined when the supine AHI was ≥ 10, in combination with a lateral AHI of < 10. In 12 patients with supine-dependent sleep apnea, an MAD reduced the supine AHI from a median of 41 to 5.9. In 14 patients with non-supine-dependent sleep apnea, the treatment reduced the supine AHI from 44 to 21 and the lateral AHI from 21 to 4.5. The adjusted odds ratio for a successful apnea reduction to an AHI of < 10 in both the supine and the lateral positions was 30 for supine-dependent sleep apnea.

Chung *et al* studied 72 consecutive patients (42 patients with and 30 without position dependent sleep apnea when applying Cartwright's POSAS criteria) who underwent a sleep study before and after insertion of an MAD.[71] They found that "patients with positional OSAS had substantially better treatment outcomes than patients with non-positional OSAS". Both the decrease in, overall and supine AHI was significantly greater in the positional OSAS group.

The role of combination therapy - MAD with PT - remains to be further elucidated, but seems promising. Cartwright showed that the "combined effect of PT and a tongue retaining device was better than one of the treatment modalities alone".[46] Sixty patients with an AHI of at least 12.5 were randomly assigned to either: (1) MAD, (2) PT (positional alarm) or (3) combination therapy (MAD and PT). The AHI was reduced from 27.4 to 11.4 in group 1, from 33.3 to 20.8 in group 2, from 30.7 to 7.9 in group 3.

Conclusion

In brief, they all conclude that MADs are more effective in patients with positional OSAS than in patients without positional OSAS.
The role of combination therapy remains to be further elucidated

Sleep position and positional therapy in combination with CPAP

As mentioned CPAP compliance is often poor. One of the many reasons for CPAP failure and noncompliance is high CPAP pressure.

Overview of the literature

In a retrospective study by Pevernagie and Shephard, patients diagnosed with OSAS returned for a second overnight sleep study, during which nCPAP was titrated up to a level that eliminated SDB events and snoring in the supine position.[72] Thirty-one patients who had sufficient sleep

time in NREM and REM sleep in both supine and non-supine sleep postures were included. They found that "patients with positional sleep apnea required less positive airway pressure, than non-positional patients, as well as a tendency to avoid sleeping on the back in direct proportion to the severity of their OSAS in that position".

In contrast, in a small-scale study, Sériès and Marc concluded that CPAP compliance improved with auto-CPAP therapy in patients with sleep stage- and/or body position dependent nocturnal breathing disorders, compared to fixed CPAP.[73] The effective pressure/time index was significantly lower in sleep stage- and body position dependent patients treated with fixed CPAP, than in the other patients.

Oksenberg *et al* concluded in a retrospective study of 83 consecutive patients undergoing nCPAP titration, that the optimal nCPAP level was significantly higher in the supine position than it was in the lateral position.[74]

Body position and sleep stage have been shown to significantly influence the positive pressure level needed to treat obstructive breathing abnormalities. Pressure level requirements may vary over time, due to several factors such as weight loss or gain, medication and alcohol use, nasal congestion, changes in jaw position (due to an MAD for example), duration of CPAP therapy (CPAP is thought to play a role in reducing edema resulting from snoring-associated vibration and apnea-induced suction of the upper airway), the cyclic alternating pattern of sleep stages or body position.[59, 71-73]

Conclusion

Most studies suggest that patients' positive pressure needed in the supine position is greater that that needed in non-supine positions. Therefore, patients benefit from auto-CPAP, with a consequent increase in compliance.

PT could theoretically be of value. The treatment of OSAS is a stepwise approach. If a patient with supine dependent OSAS can avoid the supine position, the consequent decrease in AHI and positive pressure requirements results in less aggressive treatment, improving tolerance and compliance.[75]

Sleep position and nasal expiratory device

One study was found to have examined the effect of sleep position on the efficacy of the novel treatment: the nasal expiratory resistor device (nEPAP).[76] Twenty subjects with OSAS were included in the study who underwent PSG whilst wearing the therapy. The results suggest that patients with position-dependent SDB (defined as a supine AHI greater than the lateral AHI) were more likely to have an acceptable therapeutic response to nEPAP, although the results did not reach statistical significance.

Discussion and Future Perspectives

Unfortunately, research on the effect of positional therapy on POSAS lacks good clinical trials, a miss in OSAS research in general. Not all articles included in this paper specify definitions and cut-off values used to rule in OSAS. In 1999, the American Academy of Sleep Medicine Task Force (AASM) introduced evidence based standardized scoring guidelines and cut-off values for OSAS. Studies discussed in this paper may have applied different definitions, especially if performed before 1999.[23]

At present, evidence of PT effectiveness is based on small-scale case series and a few randomized trials. Little is known about the long-term compliance of PT and the actual ability of patients to learn to avoid the supine position following PT treatment. There is room for technical improvement of the devices to reduce discomfort and consequent disruption of sleep architecture as to improve compliance. POSAS is commonly defined as a *difference of 50% or more in apnea index between supine and non-supine positions,* but many question Cartwright's criteria and apply adapted versions. Similar issues have faced CPAP compliance criteria and surgical and MAD success definitions.[60] CPAP therapy is regarded as successful if the AHI drops below 5 when CPAP is used. Current trends define compliance as 4 hours per night as an average over all nights observed.[61]

Surgical success was originally defined by Sher *et al*: AHI reduction of at least 50% and AHI reduction to below 20.[77] Others have later proposed to tighten surgical success criteria to a postoperative AHI below 15 (regarded as "clinically relevant" OSAS), below 10 and recently even below 5.[78] Patients in whom the AHI is reduced by 20%-50% are classified as responders.[12]

PT of OSAS now commonly aims to arouse the patient when lying on the back so the subject rotates the body on his/her side to alleviate respiratory obstructions. In head position-aggravated trunk supine position-dependent OSAS, it may be sufficient to stimulate the subject to rotate only the head sideways, based on a position sensor monitoring the orientation of the head. It can be expected that this would have a much less profound negative effect on sleep quality.

CONCLUSION

Research performed in the past 10 - 20 years, shows that PT has a significant influence on AHI. These studies are predominantly performed as case series on a comparably small number of patients. Still, results have not found their way into the daily diagnostic and treatment routine. An approximate 56% of patients with OSAS, have position dependent OSAS commonly defined as a *difference of 50% or more in apnea index between supine and non-supine positions*. A great deal is to be gained from treating patients with POSAS with PT. PT, often simple and inexpensive, shows promise as a stand-alone treatment or as an additional measure to increase the success rate of other, established treatment methods. Treating body position should receive more attention in the treatment of sleep apnea. Long-term compliance for PT remains an issue, and although remarkable results have been shown using innovative treatment concepts for PT, there is room for both technical improvement of the devices used and for further research.

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CHAPTER 3

Evaluation of a new simple treatment for positional sleep apnea patients

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ABSTRACT

Study objective

To evaluate the effect of a novel electronic device to treat positional sleep apnea.

Methods

Patients with polysomnographically proven positional sleep apnea were asked to participate in this study. These patients would undergo two additional polysomnographies, one with the device attached, but in *off* mode, and one with the device attached in *on* mode.

Results

30 Patients were included in this study. Most polysomnographical parameters improved significantly with the device in *on* mode. The mean AHI improved from 27.7 (no device), 23.5 (*off*) to 12.8 (*on*), percentage of total sleeping time in supine position was 40.0, 40.0 and 19.0%, the AI improved from 16.3, 11.5 to 3.4/h, the DI decreased from 11.5, 9.7 to 4.6/h and arousal index improved from 9.0, 9.9 to 6.8/h. Number of awakenings changed from 3.4, 3.9 to 4.1, but this change was non-significant.

Conclusion

This study is the first in which positional sleep apnea is effectively treated with a neck worn position device, without disturbing the sleep quality. Over 50% of OSAS patients suffer from positional OSAS, of which a significant percentage could be treated with positional therapy, either as a single treatment or in combination with other treatment modalities.

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 one from the Netherlands a remarkable steady 56% of patients have positional sleep apnea, defined as a supine AHI of at least twice as high compared to the AHI in the other positions.[21-23] 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, neck worn, device which influences the role of sleep position in sleep apnea, while getting around the problem of disrupted sleep quality.

METHODS

Study design

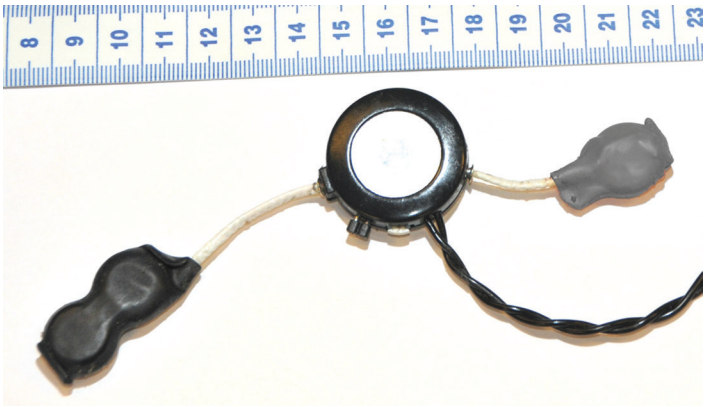
Consecutive patients, aged >18years, who were referred to the Department of Otorhinolaryngology, Head and Neck Surgery of the Saint Lucas Andreas Hospital (Amsterdam, The Netherlands) and who were diagnosed, using full overnight in-hospital polysomnography, with positional sleep apnea (AHI > 5, AHI supine ≥ 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-hospital polysomnographies after they had given written informed consent. These two test recordings were scheduled with at least one week and no more than 2 weeks 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

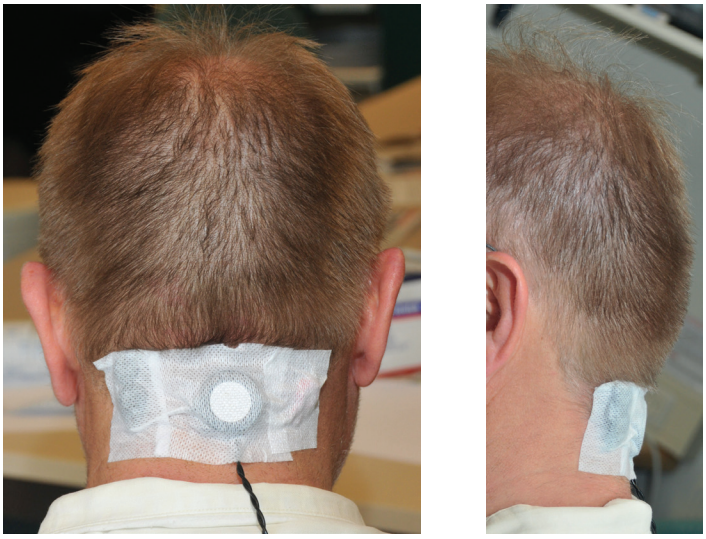
Polysomnography recordings were carried out using a digital polygraph system (Embla A10, Broomfield, USA). This records the electroencephalogram (FP2-C4/C4-O2), electrooculogram, EKG and submental and anterior tibial electromyogram. Nasal airflow was measured by a pressure sensor and arterial oxygen 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 and 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 analysed 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 3 small batteries, see figure 1(a)) 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 1(b)) and connected to the polysomnography system.



(a)



(b)

Figure 1 - (a, 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 polysomnography system. (b) shows the device attached to the skin of the neck with hypoallergenic adhesive tape.

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 or more with a reduction of oronasal airflow of >= 90 %. 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.[23] 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. Sleep was staged using the criteria according to Rechtschaffen and Kales. Deep sleep was defined as slow wave sleep (Rechtschaffen and Kales stage III and IV, or AASM Non-REM stage III).

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 the paired Student's T-Test. Some of the parameters are not strictly normally distributed.

Despite the latter, the 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 analyze 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 week 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. 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 therefore these patients were not excluded from analysis. No side effects were reported.

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

In figure 2 (a, b, 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 3 (a, b)).

Table 1 - Baseline characteristics of all patients (n=30).

Patient characteristics	
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. PSG=polysomnography.

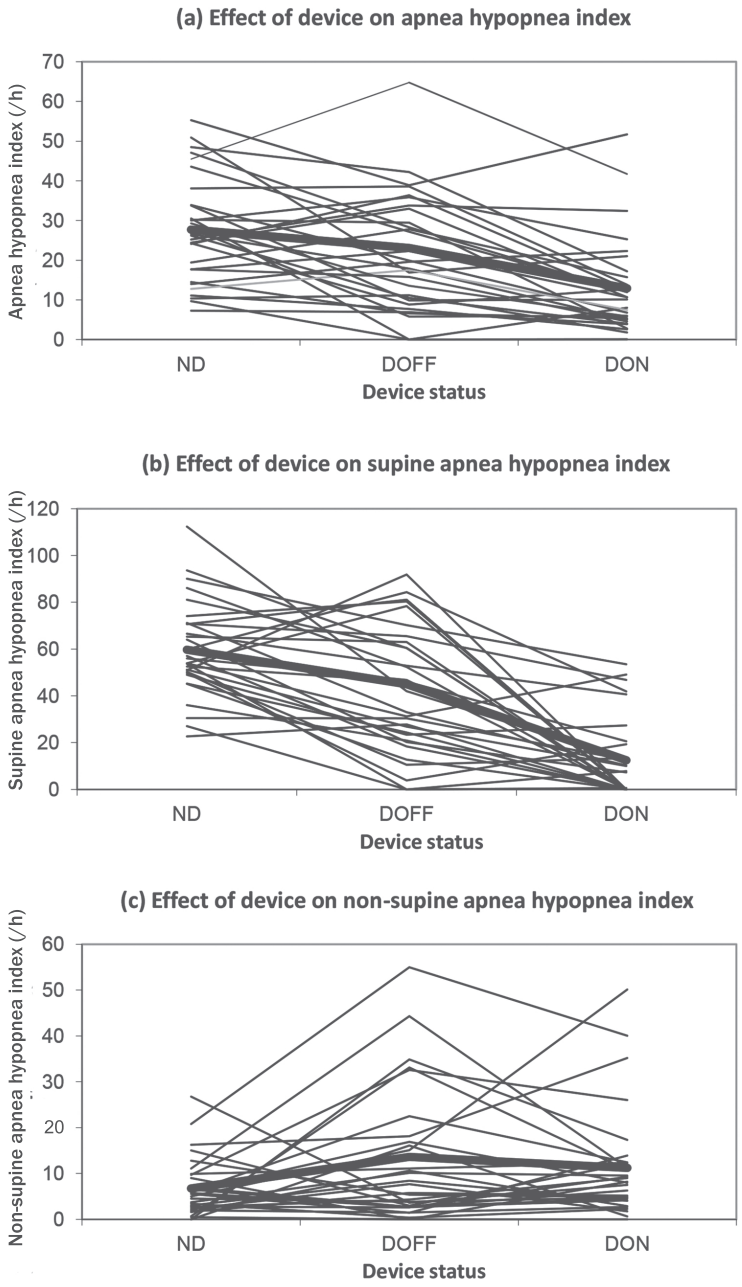


Figure 2 – Effects of device on AHI (a), supine AHI (b), non-supine AHI (c).
The bold line depicts the mean value. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus.

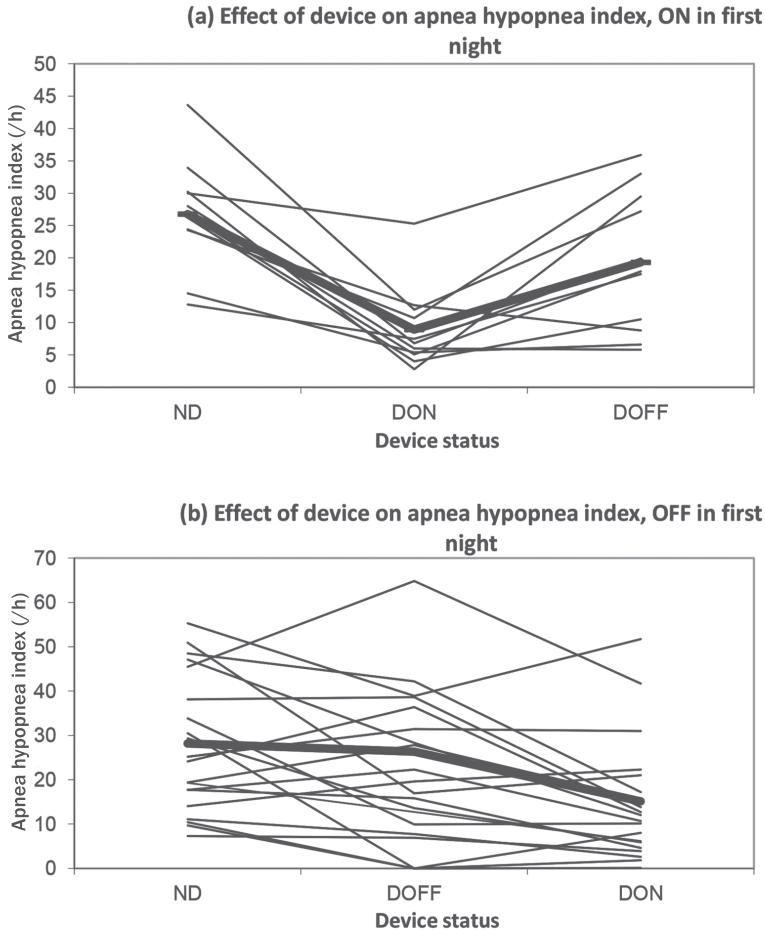


Figure 3 – Effect of device on AHI with the device ON (a) / OFF (b) during the first night.
The bold line depicts the mean value. ND=no device. DOFF=device attached in OFF modus. DON=device attached in ON modus.

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.

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).

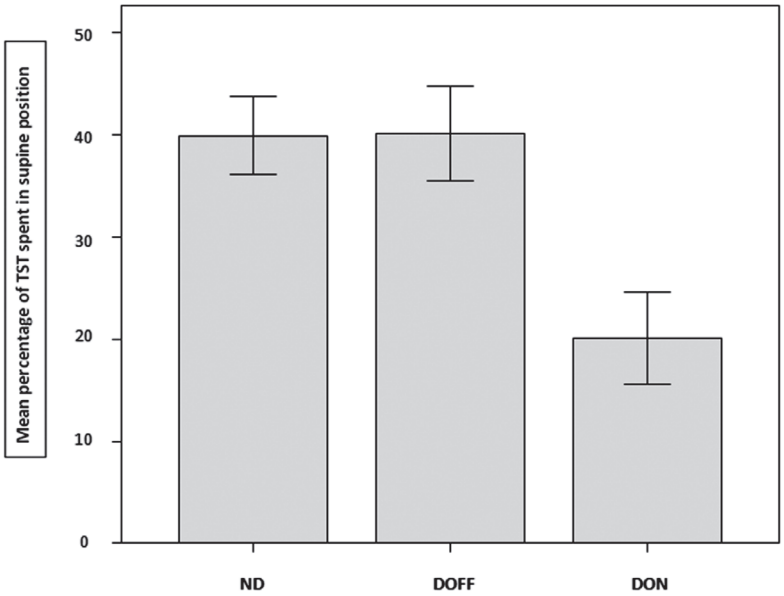


Figure 4 - Effect of device on percentage of TST in supine position.
TST=total sleep time, ND=no device, DOFF=device attached in OFF modus, DON=device attached in ON modus. The y error bars depict the standard error of the mean.

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).

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 cells=p-values <0.05. Results are shown as mean ± 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%.[22,23] 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, "shark fins", special vests,[24-27] 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.[24]

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 percentages of REM sleep, nor AHI during REM sleep were found between the 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.

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CHAPTER 4

The Sleep Position Trainer: a new treatment for positional obstructive sleep apnea

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ABSTRACT

Study objective

Positional obstructive sleep apnea syndrome (POSAS), defined as a supine apnea hypopnea index (AHI) twice or more as compared to the AHI in the other positions, occurs in 56% of obstructive sleep apnea patients. Positional therapy (PT) is one of several available treatment options for these patients. So far, PT has been hampered by compliance problems, mainly because of the usage of bulky masses placed in the back. In this article we present a novel device for treating POSAS patients.

Methods

Patients older than 18 years with mild to moderate POSAS slept with the Sleep Position Trainer (SPT), strapped to the chest, for a period of 29 +/- 2 nights. SPT measures the body position and vibrates when the patient lies in supine position.

Results

36 Patients were included, 31 patients (mean age 48.1±11.0 years; mean body mass index 27.0±3.7 $kg \cdot m^{-2}$) completed the study protocol. The median percentage of supine sleeping time decreased from 49.9% [20.4 – 77.3%] to 0.0% [range: 0.0 - 48.7%] ($p<0.001$). The median AHI decreased from 16.4 [6.6 – 29.9] to 5.2 [0.5 – 46.5] ($p<0.001$). 15 Patients developed an overall AHI below five. Sleep efficiency did not change significantly. Epworth Sleepiness Scale decreased significantly. Functional Outcomes of Sleep Questionnaire increased significantly. Compliance was found to be 100% (average use per night 6.4 ± 1.3h).

Conclusion

The Sleep Position Trainer applied for one month is a highly successful and well-tolerated treatment for POSAS patients, which diminishes subjective sleepiness and improves sleep-related quality of life without negatively affecting sleep efficiency. Further research, especially on long term effectiveness, is ongoing.

INTRODUCTION

More than half of OSAS patients appear to have position dependent OSAS (POSAS), defined as an apnea-hypopnea index (AHI) during sleep in supine position that is at least twice as high as the AHI during sleep in other positions.[1-4]

The therapeutic armamentarium for OSAS comprises several treatment options. Continuous positive airway pressure (CPAP) is often regarded as the gold standard in the treatment of moderate and severe cases. Oral appliances and upper airway surgery are both used in mild and moderate cases or in reserve of CPAP failure. In all patients with OSAS, conservative approaches including abstinence of alcohol and sedatives, weight reduction, quitting smoking and avoidance of the supine sleeping position in POSAS should be considered.[5] Positional therapy (PT) is a treatment modality which aims at preventing patients from sleeping in the worst position, which is in most cases the supine position.[6] The role of positional therapy as a minimally invasive treatment modality in patients with positional OSAS looks promising.[7] The effectiveness of positional therapy in positional OSAS has been tested since the 1980s.[8] The tennis ball technique, where a tennis ball is placed in the centre of the back, was one of the first described positional therapies and has been shown to be effective in normalizing AHI in positional OSAS patients. Several variations of the tennis ball technique (positional alarms, verbal instructions, vests, special pillows) have also been tested with similarly good results.[5,9-22] However, the clinical significance of positional therapy is so far hampered by a very low compliance rate which ranges from 40% - short term - to 10%, long term.[10,16,21] These results show the need for a positional therapy system that is able to ensure high compliance in patients suffering from POSAS and which can improve the discomfort and disruption of the sleep architecture, both being the reason for the poor compliance seen in the past. To this end, we recently presented a novel treatment concept for POSAS; a simple small neck-worn vibrating device, which corrected patients when adopting the supine position. This novel concept has shown to be effective in significantly reducing the AHI without disrupting the sleep quality.[20]

In line with this technology and its encouraging results a new medical device appropriate for wide clinical use was developed; the Sleep Position Trainer (SPT). With the SPT developed, this study aims to investigate the viability of this new vibrating device as a reliable treatment option for patients with POSAS. The hypothesis for this study states that this device presents good objective and subjective effects (respectively measured with polysomnographies and questionnaires) with a high compliance and without negatively affecting the sleep efficiency.

METHODS

Study subjects

From June 2011 through January 2012, patients who were referred to the Department of Otorhinolaryngology, Head and Neck Surgery of the Saint Lucas Andreas Hospital (Amsterdam, The Netherlands) for suspected sleep disordered breathing were considered eligible if they met the following inclusion criteria: i) age of 18 years or older; ii) AHI between 5 and 30 events/h at a baseline polysomnography; iii) positional sleep apnea defined as an AHI in supine position greater than 2 times the AHI in non-supine positions; iv) the percentage of total sleep time in supine position was between 20% and 90%; v) the percentage of central apneas was less than 50% of the total amount of apneas; vi) no medical history with known causes of daytime tiredness or sleep disruption (shift working, neurologic disorders, insomnia, periodic leg movement syndrome, narcolepsy etc); and vii) no cardiac pacemaker. Exclusion criteria were: i) use of other treatment modalities for OSAS during the course of the study; and ii) unwillingness or inability to participate in all aspects of the study. All patients signed an informed consent. The study was approved by the institution's ethics committee.

Study protocol/design

All patients underwent two polysomnographic assessments. The baseline assessment consisted of an overnight polysomnography (PSG) to confirm the diagnosis of POSAS. Within 28 days after the baseline PSG, patients started using the Sleep Position Trainer (SPT) for 29 +/- 2 nights. On day one patients filled out the Epworth Sleepiness Scale (ESS)[23] and the Functional Outcomes of Sleep Questionnaire (FOSQ)[24] to assess their daytime sleepiness and quality of life.

Treatment with the SPT was divided into three phases: a diagnostic phase, a training phase and a therapy phase. The first two nights were defined as the diagnostic phase, where the SPT monitored and recorded the sleeping position and in which no active feedback was given to the patient. The following seven nights entailed the training phase, where the SPT began to vibrate in an increasing amount of episodes of supine sleep. From night ten onwards the therapy phase started in which the SPT vibrated every time a supine sleeping position was detected in order to urge the patient to change his or her sleeping position. To promote continued use, subjects could upload and read out information about their nightly behaviour (e.g. percentages of different sleeping positions) to their own personal computer at any desired time.

The last assessment took place after 29 +/- 2 days and included a PSG whilst using the SPT. Additionally, ESS and FOSQ questionnaires were completed for a second time.

The Sleep Position Trainer Device

The Sleep Position Trainer (SPT) is a small, lightweight device (72 x 35 x 10 mm, 25 g) which is worn around the chest in a neoprene strap (Figure 1). The neoprene strap comprises a pocket in which the device is placed on the sternum and can be closed with a Velcro tab. The device measures the orientation using a three-dimensional digital accelerometer. The measurements were used to define the posture of the user; left side, right side, supine, prone or upright. The device responded

to supine position with a vibration stimulus to provide feedback to the user. The stimulus started after the supine position was detected and no turning movement was detected anymore. The device continued with a gradually increasingly strength and stimulus duration, until non-supine position was detected. If the patient did not react to the stimulus, the vibrations would be paused to be reinitiated after two minutes. Furthermore, the SPT provided an internal memory to store the sleeping posture of the user for a period of at least 90 days. The device employs a USB port to communicate data to a personal computer (PC) and to recharge the integrated battery.

Figure 1 - Subject wearing the Sleep Position Trainer.

Polysomnography

A full night diagnostic polysomnography (EMBLA® A10/Titanium, Medcare Flaga, Iceland; and Somnoscreen™, SOMNOmedics GmbH, Randersacker, Germany) was performed in each subject. To determine the stages of sleep an electroencephalogram (Fp2, C4, O2), electro-oculogram and electromyogram of the submentalis muscle were obtained. Nasal airflow was measured by a nasal cannula/pressure transducer inserted in the opening of the nostrils. Arterial blood oxyhemoglobin was recorded with the use of a finger pulse oximeter. Thoracoabdominal excursions were measured qualitatively by respiratory effort belts placed over the rib cage and abdomen. Snoring was recorded through a piezo snoring sensor. Body position was determined by a position sensor, which differentiated between the upright, left side, right side, prone and supine position. Limb movements were detected with an anterior tibial electromyogram. Electrocardiogram was also measured using two electrodes posted on the collarbone. 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. The following day, data were downloaded to the computer and analysed by dedicated sleep software (Somnologica™, Broomfield, USA; DOMINO, SOMNOmedics GmbH, Randersacker, Germany). The data were manually reviewed for analysis by an experienced sleep investigator.

Analysis and definitions

The sleep stages were scored manually in 30-s epochs according to AASM criteria, with N3 reflecting slow wave sleep or Rechtschaffen and Kales stages 3 and 4.[25] Obstructive respiratory events were analysed according to the AASM criteria.[25] As such, obstructive apnea was defined as a decrease of airflow of more than 90% for at least 10 seconds, in the presence of respiratory efforts. Central apnea was defined as a decrease of airflow of more than 90% for at least 10 seconds and no respiratory effort of the thorax or abdomen. Hypopnea was defined as a decrease of airflow of 30-90% for at least 10 seconds, with a continuation of respiratory effort and leading to a decrease in haemoglobin saturation of at least 3%. The number of apnea and hypopnea episodes per hour of sleep is referred to as the apnea-hypopnea index (AHI). Obstructive sleep apnea was diagnosed if the AHI was >5.[25] Sleep efficiency was defined as the total sleep time (TST) / time in bed (TIB).

Based on Sher's criteria of surgical success, SPT success was defined as a post-treatment AHI of less than 20 events·h^{-1} along with at least 50% decrease from the baseline AHI (responders). Treatment failure was defined as a post-treatment decrease of AHI from baseline less than 50% (non-responders).

SPT compliance, in line with CPAPs compliance definition,[26] was defined as the use of the SPT for at least four hours per night, as an average over all nights observed.

Statistical analysis

Statistical analysis was performed using SPSS (version 15, SPSS Inc, Chicago, IL). Quantitative data are reported as mean ± SD or as median [range]. Comparison of data between baseline and after one month of SPT use was carried out using the paired *t*-test in case of normally distributed data and the Wilcoxon test in case of skewed data. Data obtained during the three different phases (i.e., diagnostic, training and therapy) were compared with Friedman's test for repeated measures. A p-value of < 0.05 was considered to indicate statistical significance.

RESULTS

Thirty-six patients who met the inclusion criteria were included in the study. Thirty-one patients completed the study protocol. Five patients withdrew; three patients because of lack of motivation and two patients because of back and shoulder complaints.

The remaining 31 patients ((27 males); mean age 48.1±11.0 years; mean body mass index 27.0±3.7 kg/m^2)) finished the study uneventfully. The compliance rate was 100%, meaning that all patients used the SPT for more than 4 hours per night. Average use per patient per night was 6.4 ± 1.3 hours. The polysomnographical and clinical characteristics of patients at baseline and after one month of SPT are shown in Table 1. As the results show, the total AHI but also the AHI in supine position as well as the percentage of sleep time spent in supine position, desaturation index, apnea index and ESS score presented significant decrease, whereas minimum oxygen desaturation, the percentage of sleep time spent in non-supine position, and FOSQ score exhibited significant increase. Sleep efficiency did not change significantly. Individual values of the apnea-hypopnea index, the percentage of time spent in supine position, ESS and FOSQ scores at baseline and after one month of positional therapy are shown in Table 2.

22 Patients were considered responders (71.0%) and 9 non-responders (29.0%). The clinical and polysomnographical characteristics of responders and non-responders are presented in Table 3. AHI, apnea index, desaturation index, supine AHI and Epworth Sleepiness Scale score all significantly decreased in the responder group. Furthermore, average oxygen saturation, minimum oxygen saturation and FOSQ score significantly increased in the responder group. In the non-responder group a significant increase was seen in non-supine AHI. In both responders and non-responders a significant increase in percentage non-supine position sleeping time and a significant decrease in percentage of supine position sleeping time were seen. Percentage of N3 or deep sleep did not change significantly during SPT therapy. Responders had a significantly lower AHI, desaturation index and apnea index than non-responders after SPT ($p<0.001$, $p=0.004$ and $p=0.001$). Non-responders had a significantly higher non-supine AHI and significantly lower number of awakenings than responders after SPT ($p<0.001$ and $p=0.008$).

Figures 2 and 3 show the effect of SPT on respectively the percentage of supine position and AHI. Post-hoc analyses showed that the decrease between diagnostic and training phase was highly significant ($p<0.001$), as was the case for the decrease between diagnostic and therapy phase and between training and therapy phase (data not shown here).

Table 1 - Polysomnographical and clinical variables of the study group at baseline and after one month of SPT therapy (n=31).

	Baseline	After SPT	p-value
Age, yrs	48.1 ± 11.0		
Male sex, %	87.1		
BMI, kg/ m^2	27.0 ± 3.7	27.4 ± 4.0	0.387
Compliance rate, %		100.0	
AHI, events/h	16.4 [6.6 - 29.9]	5.2 [0.5 - 46.5]	**<0.001**
AHI in supine, events/h	35.7 [9.3 - 81.0]	0.0 [0.0 - 100.7]	**<0.001**
AHI in non-supine, events/h	3.2 [0.0 - 16.2]	4.3 [0.1 - 48.0]	0.052
Average oxygen saturation, %	95.1 ± 1.4	95.5 ± 1.6	0.101
Minimum oxygen desaturation, %	84.5 ± 4.1	88.4 ± 3.6	**<0.001**
Desaturation index, events/h	11.2 [2.2 - 22.4]	5.2 [0.9 - 39.6]	**<0.001**
Apnea index, events/h	10.4 [1.0 - 26.3]	2.5 [0.0 - 21.3]	**<0.001**
Arousal index, events/h	6.1 [0.0 - 28.4]	5.5 [0.0 - 22.8]	0.289
Number of awakenings	4.0 [0.0 - 60.0]	3.0 [0.0 - 10.0]	0.323
Total sleep time, min	456 ± 76	429 ± 87	0.187
N2 sleep/Total sleep time, %	52.0 ± 8.7	50.0 ± 12.1	0.322
N3 sleep/Total sleep time, %	22.4 ± 9.8	21.7 ± 7.7	0.618
REM sleep/Total sleep time, %	19.5 ± 5.6	20.9 ± 6.4	0.364
Sleep efficiency, %	89.1 [61.1 - 99.7]	89.4 [58.0 - 98.6]	0.544
Percentage supine	49.9 [20.4 - 77.3]	0.0 [0.0 - 48.7]	**<0.001**
Percentage non-supine position	50.1 [22.7 - 79.6]	100.0 [51.3 - 100.0]	**<0.001**
ESS score	11 [2 - 20]	9 [0 - 19]	**0.004**
FOSQ core	86.0 ± 22.1	93.8 ± 21.7	**0.001**

Data are presented either as mean ± SD or as median [range]. SPT: Sleep Position Trainer.

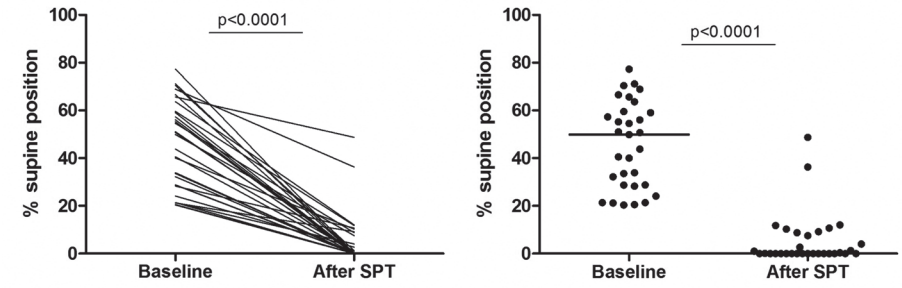
Table 2 - Individual values of apnea-hypopnea index, percentage of supine position, and Epworth Sleepiness Scale scores of all patients at baseline and after one month of SPT therapy.

Patient No	AHI		% supine position		ESS		FOSQ	
	Baseline	After SPT	Baseline	After SPT	Baseline	After SPT	Baseline	After SPT
1	6.6	3.3	63.6	12.0	19	19	88	88
2	12.1	5.2	20.5	0.0	16	9	77	78
3	20.2	15.5	65.6	48.7	2	2	85	99
4	16.2	1.8	32.2	0.0	17	18	36	40
5	21.0	10.2	40.0	10.3	14	10	48	72
6	19.0	9.9	28.8	0.1	11	5	90	111
7	20.8	15.4	24.1	2.7	18	19	71	62
8	11.0	10.1	40.5	0.0	12	13	84	92
9	21.0	16.0	56.0	0.0	10	7	101	101
10	11.7	4.3	77.3	0.0	12	12	97	97
11	10.4	0.5	28.7	0.0	17	3	108	118
12	13.4	4.5	70.4	1.3	4	4	111	116
13	24.0	3.5	59.0	0.0	6	3	91	101
14	23.4	9.6	33.5	0.0	15	14	66	74
15	14.5	6.9	21.4	0.0	3	3	119	119
16	16.2	7.6	49.9	7.5	15	13	63	86
17	27.5	4.7	54.5	8.8	5	1	75	80
18	11.8	3.1	20.4	0.0	9	10	73	76
19	18.3	48.4	21.4	4.0	8	4	90	74
20	16.0	19.5	43.8	1.0	7	8	112	120
21	11.9	3.3	57.3	0.0	20	16	82	114
22	29.8	1.9	50.7	0.4	18	9	55	99
23	29.9	8.8	21.2	9.2	12	13	64	75
24	11.1	6.9	71.1	0.0	9	12	59	56
25	6.8	4.9	33.9	0.0	5	0	118	109
26	21.2	2.1	59.5	11.8	11	2	104	120
27	16.6	5.4	68.9	36.3	16	19	105	113
28	11.5	2.0	28.3	10.7	4	1	122	122
29	18.3	1.6	66.5	0.0	8	9	100	108
30	22.9	8.9	55.2	0.0	5	5	70	75
31	10.8	0.7	51.0	0.0	11	4	102	114

Table 3 - Anthropometrical data, and clinical and polysomnographic variables in responders and non-responders at baseline and after one month.

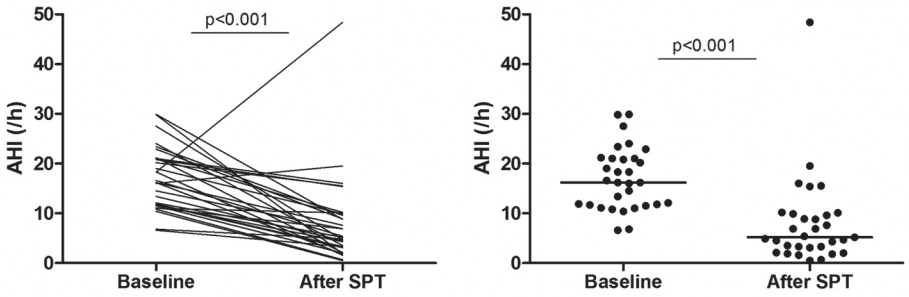
	Responders (n=22)			Non-responders (n=9)			
	Baseline	**After SPT**	**p-value#**	**Baseline**	**After SPT**	**p-value#**	**p-value***
Age, yrs	49.8 ± 11.6			44.1 ± 8.6			
Male sex, %	86.4			88.9			
BMI	27.3 ± 3.4			26.3 ± 4.6			
Compliance rate, %		100.0			100.0		
Average SPT use per night, min		400.2 ± 154.4			412.9 ± 125.1		
AHI, events/h	16.2 [6.6 - 29.9]	3.9 [0.5 - 10.3]	**<0.001**	18.2 [6.7 - 21.0]	14.1 [4.9 - 46.5]	0.214	**<0.001**
AHI in supine, events/h	36.5 [9.3 - 81.0]	0.0 [0.0 - 37.3]	**<0.001**	34.7 [14.9 - 63.6]	0.0 [0.0 - 100.7]	0.173	0.685
AHI in non-supine, events/h	3.2 [0.0 - 16.2]	3.2 [0.1 - 9.6]	0.833	3.7 [0.2 - 9.1]	10.1 [3.5 - 48.0]	**0.011**	**<0.001**
Average oxygen saturation, %	95.0 ± 1.5	95.5 ± 1.4	**0.004**	95.4 ± 1.0	95.2 ± 2.0	0.681	0.620
Minimum oxygen desaturation, %	84.4 ± 4.5	89.4 ± 2.3	**<0.001**	84.7 ± 3.4	86.0 ± 5.1	0.431	0.087
Desaturation index, events/h	11.2 [2.2 - 22.4]	4.6 [0.9 - 13.1]	**<0.001**	11.6 [5.5 - 19.0]	8.5 [3.4 - 39.6]	0.213	**0.004**
Apnea index, events/h	11.0 [2.2 - 26.3]	1.8 [0.0 - 7.3]	**<0.001**	8.0 [1.0 - 19.4]	8.3 [1.6 - 21.3]	0.953	**0.001**
Arousal index, events/h	7.5 [3.0 - 28.4]	5.2 [0.0 - 20.5]	**0.027**	0.0 [0.0 - 18.5]	6.5 [0.0 - 22.8]	0.176	0.203
Number of awakenings	3.5 [0.0 - 60.0]	4.0 [1.0 - 10.0]	0.659	4.0 [0.0 - 15.0]	1.0 [0.0 - 9.0]	0.068	**0.008**
Total sleep time, min	466 ± 80	433 ± 94	0.218	432 ± 63	418 ± 68	0.666	0.656
N2 sleep/Total sleep time, %	49.8 ± 8.2	47.3 ± 12.2	0.366	57.3 ± 8.0	56.6 ± 9.5	0.700	0.051
N3 sleep/Total sleep time, %	24.7 ± 9.3	23.6 ± 7.4	0.518	16.7 ± 8.8	17.1 ± 6.8	0.846	**0.032**
REM sleep/Total sleep time, %	19.3 ± 5.9	21.0 ± 7.1	0.348	20.1 ± 5.1	20.6 ± 4.4	0.858	0.891
Sleep efficiency, %	88.6 [61.1 - 99.7]	86.1 [58.0 - 98.6]	0.306	89.1 [70.1 - 96.0]	92.0 [68.9 - 98.1]	0.594	0.086
Percentage supine	50.9 [20.4 - 77.3]	0.0 [0.0 - 36.3]	**<0.001**	40.5 [21.4 - 71.1]	0.1 [0.0 - 48.7]	**0.008**	1.000
Percentage non-supine position	49.2 [22.7 - 79.6]	100.0 [63.7 - 100.0]	**<0.001**	59.5 [29.0 - 78.6]	99.9 [51.3 - 100.0]	**0.008**	0.881
ESS score	12 [3 - 20]	9 [1 - 19]	**0.007**	9 [2 - 18]	7 [0 - 19]	0.291	0.623
FOSQ core	84.4 ± 23.6	94.8 ± 21.8	**<0.001**	90.0 ± 18.6	91.6 ± 22.6	0.710	0.715

Data are presented either as mean ± SD or as median [range]. SPT: Sleep Position Trainer. #Comparing baseline values with values after SPT per group responders/non-responders. *Comparing responders with non-responders after SPT.



a) b)

Figure 2 - Effect of SPT therapy on percentage of supine sleeping time.
a) Lines depict individual changes in percentage of supine sleeping time from baseline to after one month of SPT therapy.
b) Dots depict individual percentages of supine sleeping time. The horizontal black lines show the median.
SPT= Sleep Position Trainer



a) b)

Figure 3 - Effect of SPT therapy on AHI.
a) Lines depict individual changes in AHI from baseline to after one month of SPT therapy.
b) Dots depict individual AHI values. The horizontal black lines show the median.
SPT= Sleep Position Trainer, AHI= apnea hypopnea index

DISCUSSION

If one would set requirements for an ideal (P)OSAS treatment, it would be effective, well tolerated, it would not disturb sleep or would even improve it, it would be reversible, would have negligible side effects, at acceptable costs. The analysis of more than 900 sleep nights in this study indicates that the SPT fulfils these six criteria to a high degree.

This study shows that the SPT is highly effective in the treatment of POSAS. The percentage of time slept in supine position decreased significantly, with a median of zero percent. When Sher's criteria of surgical success were used (i.e. the responder group), a 71.0% (22/31) success rate was achieved with a median decrease of 61.1% in AHI value. Six out of nine non-responders had an AHI reduction between 20% and 50%. With this novel treatment 15 patients dropped in AHI value below five and had their (P)OSAS cured (table 2). The study of van Maanen et al.[20] showed a 60% success rate with a decrease of 53.8% in AHI value. The mean reduction in AHI was similar in both studies. Apparently, the location of the device, neck or chest, and duration of usage does not influence the average reduction in AHI. Table 4 shows the comparison between the first generation device and the SPT.

Even the most effective medical devices only form a successful treatment when used properly. CPAP is used in moderate and severe OSAS. Many patients refuse or simply cannot tolerate CPAP; about 25% of patients quit the probationary period.[27] Others use CPAP for a few hours per night, every night or incidental.[28] Treatment with oral appliances is reasonably effective in mild and moderate OSAS and snoring but can have negative side effects such as jaw discomfort, hypersalivation or dry mouth, while in the long term dental occlusion might change. In addition, up to one-third of patients have contraindications for using oral appliances.[29]

In this study compliance was defined as the use of the SPT for at least 4 hours per night, as an average over all nights observed, in line with CPAPs compliance definition.[26] The compliance, in a study period of 29 +/- 2 nights, was 100%, which is an exceptionally high rate in comparison to CPAP, oral device therapy or to other studies which researched compliance in positional therapy during one month. Ineffectiveness, backaches, discomfort and no improvement in sleep quality or daytime alertness have been responsible for poor compliance in positional therapy in the past. In this study, compliance was enhanced by using a very small, comfortably fitting device with optimal physical movement freedom. Increased comfort was further supported by several algorithms like a sleep-in period and a training program so that patients gradually could get used to sleeping in non-supine positions. In addition, patients were able to check their progress by viewing the data on their nightly behaviour on a personal computer. Improving compliance in PT is a major step forward since the recent study by Permut et al., which showed that positional therapy was equal to CPAP in normalizing the AHI in patients with mild to moderate POSAS.[17] Also positive predictions have been made about the learning effect of PT. Cartwright et al. suggested that patients may learn to avoid the supine position following PT and therefore do not need to use PT on a regular basis. Others may need PT either periodically to reinforce training or consistently to ensure non-supine sleep.[8]

As discussed briefly in an earlier section, compliance is very likely related to improvement in sleep quality, daytime alertness and treatment comfort. Sleep efficiency was not disrupted by using the SPT nor was the percentage of deep sleep. Arousal index and number of awakenings both showed a non-significant decrease. Subjective parameters like the ESS showed a significant decrease, whereas the FOSQ significantly increased, which means that patients experienced less daytime sleepiness and a higher level of sleep-related quality of life. This finding, the significant effect on ESS and FOSQ scoring, partly might be influenced by the feedback from the device (for example a computer read out of the percentage of supine sleep time) when using the therapy.

Due to the built-in training period of the SPT, patients can gradually get used to the lateral and prone position. However, 2 out of 36 patients suffered from back and shoulder complaints and consequently discontinued SPT therapy. Fortunately, when a patient has no beneficial effects or has side effects of the device, the treatment is reversible without harming the patient, unlike surgery. Another advantage is the acceptable costs for the SPT. It is a one-time purchase, which is expected to be cheaper than CPAP. In case CPAP or PT is ineffective, it presumably can be returned to the distributor. Oral devices however are custom made and in case of failure, cannot be returned and used by another patient.

There are several limitations of this study that need to be addressed. First of all, the average percentage of total time spent in supine position changed significantly from 45.6 to 5.3%, with a median of 0%; 16 out of 31 patients did not sleep in supine position anymore using the SPT. One of the reasons the average percentage did not reach zero might be the finding that 2 patients did not respond very well to the stimulus; they were able to sleep in supine position for 48.7 and 36.3% of total sleep time (table 2). Sleep position was measured in position sensors placed on the trunk (one for the PSG, one for the SPT). The finding that the occurrence of obstructive sleep apnea depends not solely on the position of the trunk but also on the position of the head has already been discussed earlier by van Kesteren et al. Also, in patient 19 (Table 2) it would have been interesting to have investigated the position of the head in the polysomnographies as the AHI in lateral position was much higher in the second PSG compared to the first PSG (data not shown here), whilst percentage of supine sleep time significantly decreased.

As described in the literature, long-term results are disappointing in PT because of lack of compliance. In this study patients used the SPT for 29 +/- 2 days, therefore long-term (>6 months) effects, compliance, side effects and benefits are yet unknown. The data of this study showed that some people learned to avoid supine position rapidly, while others did not seem to have such a therapeutical effect, or at least not within the study period of one month. Further research is ongoing, concentrating on long-term compliance and data collection from a larger group of subjects.

Table 4 - Comparison of first generation device versus SPT.

	First generation	SPT
Device placement	Neck (Taped)	Chest (strapped)
Vibrational stimulus	Yes	Yes
Timing vibrational stimulus	After 30 seconds	Directly
Varying in frequency	No	Yes
Varying in amplitude	Yes	Yes
Training program	No	Yes
Start delay	No	Yes
Data viewing feedback system	No	Yes

CONCLUSION

This study shows that the Sleep Position Trainer applied for one month i) cures (P)OSAS in 48% of patients (15/31) ii) is a well-tolerated treatment for patients with positional OSAS with a very high compliance, iii) is associated with a response rate of 71.0% and a median decrease of AHI of 61.1% (in subjects who completed the one month study), iv) reduces the percentage of total sleeping time spent in supine position to a median of zero, v) does not negatively affect sleep quality and vi) diminishes subjective sleepiness and improves sleep-related quality of life.

In conclusion, it appears that the SPT applied for one month is a highly successful and well-tolerated treatment for patients with positional OSA, which diminishes subjective sleepiness and improves sleep-related quality of life without disrupting sleep quality. Further research, especially on long-term results, is ongoing.

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CHAPTER 5

Long-term effectiveness and compliance of positional therapy with the Sleep Position Trainer in the treatment of positional obstructive sleep apnea syndrome

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ABSTRACT

Study objective

To investigate effectiveness, long-term compliance, and effects on subjective sleep of the Sleep Position Trainer (SPT) in patients with position-dependent obstructive sleep apnea syndrome (POSAS).

Methods

Prospective, multicenter cohort study. Adult patients with mild and moderate POSAS were included. Patients would use the SPT for 6 months. At baseline and after 1, 3, and 6 months, questionnaires would be completed: Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Functional Outcomes of Sleep Questionnaire (FOSQ), and questions related to SPT use.

Results

One hundred forty-five patients were included. SPT use and SPT data could not be retrieved in 39 patients. In the remaining 106 patients, median percentage of supine sleep decreased rapidly during SPT's training phase (day 3 to 9) to near-total avoidance of supine sleep. This decrease was maintained during the following months of treatment (21% at baseline versus 3% at 6 months). SPT compliance, defined as more than 4 h of nightly use, was 64.4%. Regular use, defined as more than 4 h of usage over 5 nights/week, was 71.2%. Subjective compliance and regular use were 59.8% and 74.4%, respectively. Median ESS (11 to 8), PSQI (8 to 6), and FOSQ (87 to 103) values significantly improved compared with baseline.

Conclusion

Positional therapy using the Sleep Position Trainer (SPT) effectively diminished the percentage of supine sleep and subjective sleepiness and improved sleep related quality of life in patients with mild to moderate position-dependent obstructive sleep apnea syndrome. SPT treatment appeared to have sustained effects over 6 months. SPT compliance and regular use rate were relatively good. Subjective and objective compliance data corresponded well. The lack of a placebo-controlled group limited the efficacy of conclusions.

INTRODUCTION

Positional obstructive sleep apnea syndrome (POSAS) occurs in approximately 56% of patients with OSAS[1,2] and is defined as an apnea-hypopnea index (AHI) greater than 5 and an AHI in the supine position twice as high or more when compared with AHI in nonsupine positions together with subjective complaints.[3] POSAS correlates negatively with body mass index (BMI) and OSAS severity.[4] Methods to avoid the supine sleeping position, i.e., positional therapy (PT), in whichever form, have a substantial influence on OSAS severity.[5] PT with a bulky mass placed against the patient's back has proved to be as effective as continuous positive airway pressure (CPAP) in reducing AHI in patients with mild (5 < AHI < 15) and moderate (15 < AHI < 30) POSAS.[6] Recently, the Sleep Position Trainer (SPT), a new form of PT, has been introduced. It has been shown to reduce the average percentage of supine sleep time from 45.6% to 5.3% and to cure (defined by an AHI < 5.0) 48% of patients with mild and moderate POSAS. Furthermore, patients report that it is less bulky and more comfortable to wear.[7] Most of the currently available prospective studies investigating PT in patients with POSAS have studied short-term effects on AHI and/or subjective sleep parameters during 1 day, week, or month of use.[8-13] However, it is a clinical reality that most OSAS treatment options in which a device has to be applied (CPAP, mandibular advancement device (MAD), PT) suffer from long-term compliance problems and hence hamper therapeutic effectiveness.[14-16] The aim of the current study was to investigate the effectiveness, long-term compliance, and effects on subjective sleep parameters in a group of patients with POSAS using the SPT for a period of 6 months.

METHODS

Patients

From February through August 2012, participants were consecutively recruited from 18 major sleep clinics in the Netherlands for an implementation cohort study. Adult participants, in whom no longer than 3 months earlier a diagnosis of mild or moderate POSAS had been made by means of a polysomnography (PSG) and who could be followed up digitally and were computer literate, were included. Exclusion criteria included any prior (P)OSAS treatment, central sleep apnea, uncontrolled or serious illness (i.e., cancer, chronic heart failure (New York Heart Association (NYHA) class II and higher), chronic obstructive pulmonary disease (Global initiative for chronic Obstructive Lung Disease (GOLD) stage II and higher), any other comorbid sleep disorder (for example narcolepsy, parasomnia, periodic limb movement disorder, restless legs syndrome, or primary insomnia), seizure disorders, cardiac pacemaker, mental retardation, current psychiatric disorders (i.e. substance related disorders and psychotic, mood, anxiety, somatoform, factitious, impulse control and adjustment disorders), or physical problems causing inability to sleep on the side. The baseline visit consisted of a medical history and physical examination by the on-site physician investigator. Inclusion consisted of enrolment in an online database. A Dutch medical device distributor company contacted and visited the included patient to deliver the SPT and instruct the patient on its use. The patient was assigned an account online to upload SPT data after registration of his or her SPT in the online database. The online inclusion system digitally sent the following questionnaires to all registered subjects at baseline, and after the first, third, and sixth month of use: Epworth Sleepiness Scale (ESS, range 0-24),[17] Pittsburgh Sleep Quality Index (PSQI, range 0-21),[18] and the Functional Outcomes of Sleep Questionnaire (FOSQ, range 0-120).[19] Patients would use the SPT for 6 months and could keep their device after the study period ended. Patients could stop using the SPT at any time. This study was centrally approved by the Medical Ethics Committee (Amsterdam), followed by local committees. All participants signed informed consent prior to the initiation of any research activities.

Polysomnography

PSG recordings were carried out on site using a digital polygraph system. This system recorded the electroencephalogram, electrooculogram, electrocardiogram, and submental and anterior tibial electromyogram results. Nasal airflow was measured using a pressure sensor and arterial oxygen saturation by finger pulse oximetry. Thoracoabdominal motion was recorded by straps containing piezoelectric transducers. Snoring was recorded using a piezo snoring sensor. Body position was determined using a position sensor, which was attached to the midline of the abdominal wall. This sensor differentiated between the upright, left side, right side, prone, and supine positions. Data were downloaded to the computer and analysed by dedicated sleep software and manually reviewed for analysis by an experienced on-site sleep investigator.

Sleep Position Trainer

The SPT has been described earlier[7] and consisted of a small, lightweight device (72 × 35 × 10 mm, 25 g) that was worn across the chest with a neoprene strap (Figure 1). The device used a three-dimensional digital accelerometer to determine body position. A video-based validation

study by the manufacturer showed that SPT has an accuracy of 96.3% in the measurement of body position during 167 body position turns.[20] Treatment with the SPT was divided into three phases: a diagnostic phase, a training phase, and a therapy phase. The first 2 nights were defined as the diagnostic phase, during which the SPT monitored and recorded the sleeping position and no active feedback was given to the patient. The following 7 nights entailed the training phase, during which the SPT began to vibrate in an increasing amount of episodes of supine sleep. Night 10 onward comprised the therapy phase, during which the SPT vibrated every time a supine sleeping position was detected in order to urge the patient to change his or her sleeping position. The vibration stimulus was adapted automatically in strength, pattern, and duration, until a nonsupine position was detected. If the patient did not react, the vibrations were paused and reinitiated after 2 min. Furthermore, the SPT provided an internal memory to store data on sleeping posture and a USB port to recharge the integrated battery and to communicate data to an online self-monitoring system, which also enabled distance monitoring by the patient's physician.

Figure 1 - The Sleep Position Trainer.

Definitions

The criteria for OSAS included an AHI of 5 or more and evidence of daytime sleepiness. The AHI was defined as the mean number of apneas and hypopneas per hour during sleep, and an apnea as a period of 10 sec or more with a reduction of oronasal airflow of greater than 90%. Hypopnea was defined as an episode of greater than 30% reduced oronasal airflow for 10 sec or more accompanied by a decrease of 4% or more of the arterial oxyhemoglobin saturation. AHI thresholds were 5, 15, and 30 events per hour for mild, moderate, and severe levels of OSAS,[21] respectively. POSAS was defined as an AHI of 5 or higher and an AHI in the supine position at least twice as high when compared to each of the AHI values found in the other positions[22] Effectiveness was defined in relation to percentage of supine sleep time. The SPT would be considered effective when the use of the device would provide a clinically significant reduction in percentage of supine

sleep time. Compliance, in line with CPAP's compliance definition, was defined as the continuous use of the SPT for at least 4 h per night, as an average over all nights observed. Additionally, regular SPT use was defined as at least 4 h of SPT usage on 70% of the days monitored, in line with CPAP's criteria for regular use.[23] Objective data on compliance were obtained through means of the SPT on a day-to-day basis. Subjective compliance was measured using online questionnaires after 1, 3, and 6 months with the questions "How many hours do you use the SPT per night?" and "How many days per week do you use the SPT?"

Statistical analysis

Changes in parameters before and after treatment were tested with the Wilcoxon signed rank test. A P value < 0.05 was considered to be significant. All statistical analyses were performed with SPSS statistics software (version 20, IBM Corporation, Chicago, Illinois, USA). To evaluate the effects of SPT, a per-protocol analysis was performed.

RESULTS

A total of 145 patients with mild and moderate POSAS, who met the inclusion criteria, were initially included in our study and entered into the online database. Baseline patient characteristics of those 145 patients are shown in Table 1. All patients filled in the questionnaires (T = 0), which resulted in the baseline questionnaire scores depicted in Table 2. A patient flow diagram is depicted in Figure 2.

Table 1 - Patient characteristics at baseline inclusion polysomnography (n = 145).

Variable	Median
AHI (/h)	11.5 [9.0]
AHI supine (/h)	28.2 [25.6]
% supine sleep	35.0 [29.0]
Age (years)	53 [14.3]
BMI (kg/m^2)	27.0 [4.0]
Ratio male : female	4.7 : 1

AHI=apnea hypopnea index, BMI=body mass index.
Values between brackets represent the interquartile range.

Table 2 - Questionnaire values and percentage of supine sleep time during 6 months of Sleep Position Trainer treatment for all available Sleep Position Trainer users.

	N	T = 0	N	T = 1 m	N	T = 3 m	N	T = 6 m
Variable		**Median**		**Median**		**Median**		**Median**
ESS	145	11 [8]	114	8 [8]	104	8 [8]	90	8 [6]
FOSQ	145	87 [30]	114	98 [30]	103	99 [32]	90	103 [30]
PSQI	144	8 [6]	113	6 [5]	102	6 [6]	88	6 [6]
% supine	104	21 [30]	94	2 [5]	75	2 [5]	53	3 [5]

ESS=Epworth sleepiness scale, FOSQ=functional outcomes of sleep questionnaire, PSQI=Pittsburgh sleep quality index.
Values between brackets represent the interquartile range.

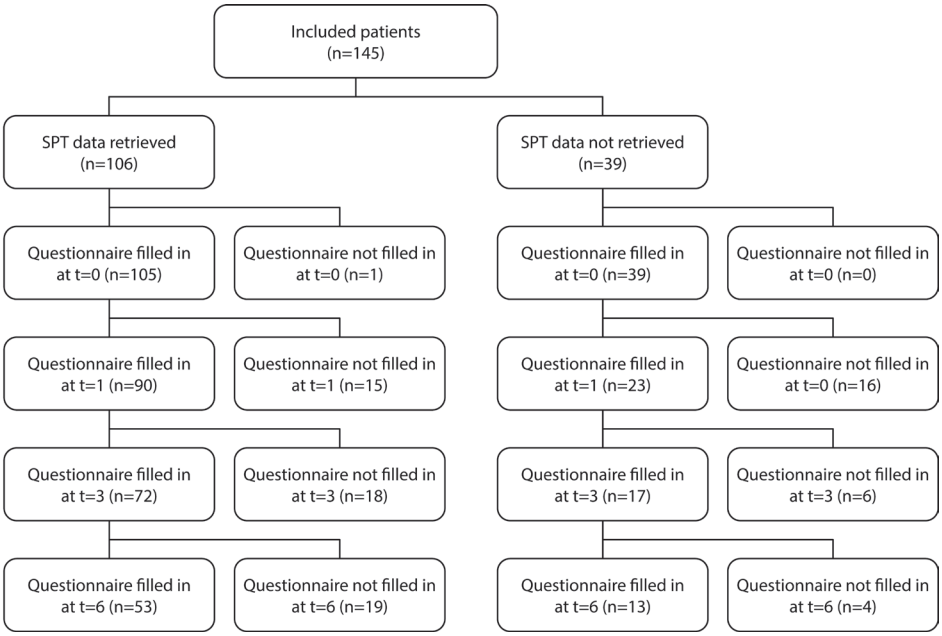

Figure 2 - Patient flow diagram.
Baseline (t = 0), one month (t = 1), 3 months (t = 3), 6 months (t = 6).

Objective compliance and hours of use

Of the initial 145 patients, neither SPT use nor SPT data could be retrieved in 39 of them because patients had not registered their SPT in the online database and were lost to follow-up. When reviewing inclusion data for these 39 patients, no significant differences could be found in terms of baseline patient characteristics when compared to the group of patients that registered their SPT. For the group of 106 patients that did upload their SPT data, the distribution of hours of SPT use is shown in Table 3. Median SPT use during 6 months was 923 h (interquartile range [IQR] = 760], or 5.5 h on average per night for all nights. As shown in Table 4, 35 patients used the SPT during all 168 nights. Median SPT use for the 106 patients was 163 of the 168 days (IQR = 98). Figure 3 shows the gradual decrease in the number of patients from whom SPT data could be retrieved and shows the eventual number of patients who were using the SPT and uploading the data during the full study period. Objective SPT compliance in this group of 106 patients, defined as more than 4 h of usage per night as an average over 168 nights, was 64.4%. Regular SPT use was 71.2% over all nights observed.

Table 3 - Distribution of hours of Sleep Position Trainer use (N = 106).

Hours of use	N	% of patients	Cumulative % of patients
1250 -1509	10	9.6%	9.6%
1000 - 1249	32	30.8%	40.4%
750 - 999	23	22.1%	62.5%
500 - 749	8	7.7%	70.2%
250 - 499	15	14.4%	84.6%
0 - 249	16	15.4%	100%
Total	104	100%	
Missing	2		

Table 4 - Distribution of days of Sleep Position Trainer use (N = 106).

Days used	N	% of patients	Cumulative % of patients
168	35	33.0%	33.0%
161 - 167	19	17.9%	50.9%
101 - 160	13	12.3%	63.2%
51 - 100	19	17.9%	81.1 %
10 - 51	10	9.4%	90.6%
0 - 9	10	9.4%	100%
Total	106	100%	

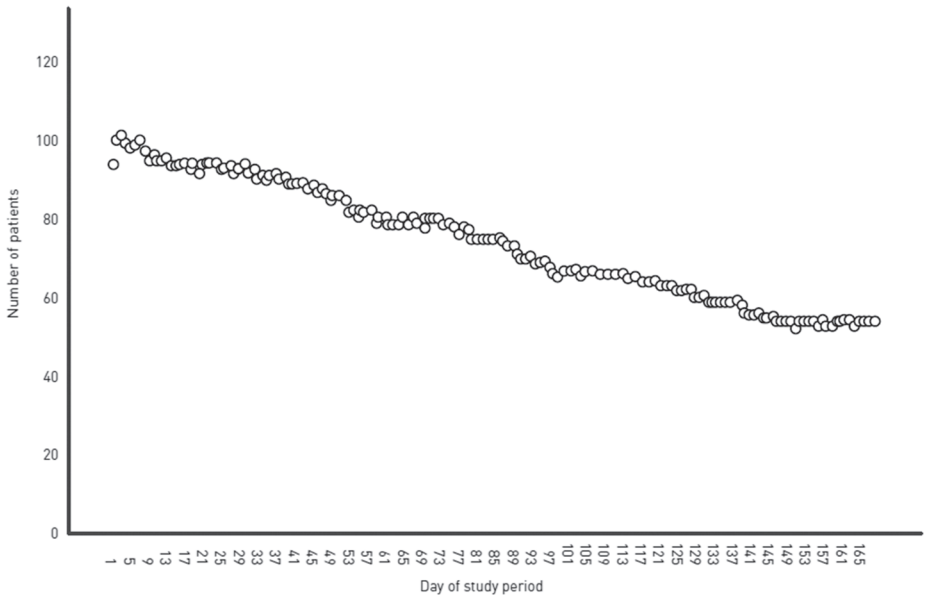

Figure 3 - Patients who used the SPT nightly for 1 h or more during the study period.

Effectiveness and effect on subjective sleep parameters

Figure 4 illustrates that the median percentage (and IQR) of supine sleep time, as measured by the SPT, quickly decreases from baseline to day 9 and that this reduced percentage of supine sleep is maintained over time. The SPT's diagnostic and training (day 1 and 2, and 3 to 9, respectively) and therapeutic phase (from day 10 onward) can be clearly identified from Figure 4. Table 2 shows median questionnaire scores and percentage of supine sleep with IQR values for all available SPT users at the different time points. According to test-by-test exclusion approach on missing data, all parameters showed a significant decrease when compared to baseline. The median percentage of supine sleep time decreased significantly from 21% to 2% after 1 month ($Z = -8.015$; $P < 0.001$), to 2% after 3 months ($Z = -7.473$; $P < 0.001$) and to 3% after 6 months ($Z = -6.251$; $P < 0.001$). ESS values significantly decreased from 11 to 8 after 1 month ($Z = -6.291$; $P < 0.001$), to 8 after 3 months ($Z = -6.647$; $P < 0.001$), to 8 after 6 months ($Z = -6.749$; $P < 0.001$). FOSQ significantly increased from 87 to 98 after 1 month ($Z = -5.874$;$P < 0.001$) to 99 after 3 months ($Z = -5.865$; $P < 0.001$) to 103 after 6 months ($Z = -6.063$; $P < 0.001$). PSQI significantly decreased from 8 to 6 after 1 month ($Z = -3.922$; $P < 0.001$), to 6 after 3 months ($Z = -4.329$; $P < 0.001$) to 6 after 6 months ($Z = -4.410$; $P < 0.001$).

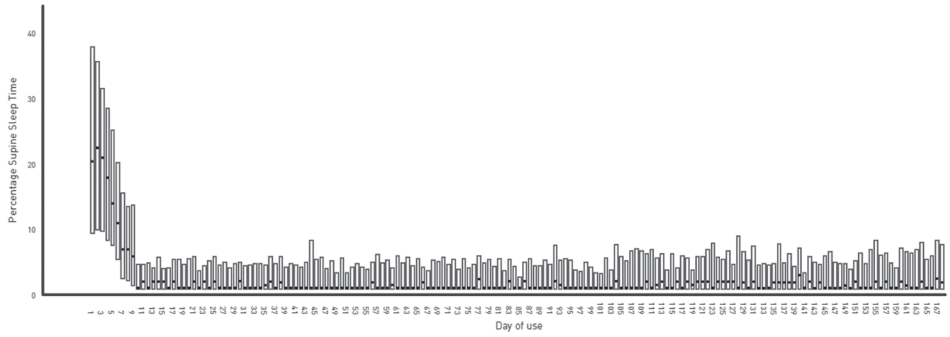

Figure 4 - Median percentage of sleep time in the supine position per night.

Subjective compliance

Data on self-reported continued use were obtained using the online questionnaires at three time points. After 1 month of therapy, subjective compliance (> 4 h per night, 7 days per w) was 91.8% (N = 110). After 3 months of therapy 74.3% of the patients were self-reportedly compliant (N = 101) and after 6 months the subjective compliance was 59.8% (N = 87). Subjective regular SPT use (> 4 h per night, 5 days per w) was 96.4%, after 3 months and 89.1% and 74.4% after 6 months.

Follow-up cohort

Of the 106 patients, we chose to further analyze all patients for whom complete records could be collected. Questionnaire scores and percentage of supine sleep time of these 53 patients are shown in Table 5. Distribution of hours of SPT use is shown in Table 6. Median SPT use during 6 months was 1127 h [IQR = 191], or 6.7 h on average per night for all nights. Objective SPT compliance in this group of 53 patients (>4 h per night, 7 days per w) was 100%.

Table 5 - Questionnaire values and percentage of supine sleep time during 6 months of Sleep Position Trainer treatment (N = 53).

	T = 0	T = 1 m	T = 3 m	T = 6 m
Variable	**Median**	**Median**	**Median**	**Median**
ESS	11 [6]	9 [8]	8 [8]	7 [6]
FOSQ	91 [29]	98 [19]	99 [27]	103 [21]
PSQI	7 [5]	5 [4]	6 [5]	6 [6]
% supine	21 [30]	2 [4]	2 [5]	3 [5]

ESS=Epworth sleepiness scale, FOSQ=functional outcomes of sleep questionnaire, PSQ=Pittsburgh sleep quality index. Values between brackets represent the interquartile range.

Table 6 - Distribution of hours of Sleep Position Trainer use (N = 53).

Hours of use	N	% of patients
0 - 249	0	0%
250 - 499	0	0%
500 - 749	0	0%
750 - 999	13	25%
1000 - 1249	30	57%
1250 -1509	10	19%
Total	53	100%

DISCUSSION

This is the first long-term follow-up study to evaluate a large group of patients with POSAS sleeping with the SPT during a period of 6 months. The main finding is that selected patients with mild to moderate POSAS can be effectively treated with the SPT, reducing the percentage of supine sleep time persistently over the course of 6 months. In concordance with our previous study,[7] sleeping with the SPT diminishes subjective sleepiness and improves sleep related quality of life in patients with mild to moderate POSAS (Table 4). The long-term decrease in median ESS from 11 (considered sleepy) to 8 (considered normal) in our group of patients with mild and moderate POSAS seems comparable to subjective sleep results using the ESS in patients with mild and moderate OSA using CPAP (mean ESS decrease from 10 to 8 in 6 months).[24] Effectiveness of PT and of PT using the SPT in terms of AHI decrease for patients with POSAS has been demonstrated before.[6,7] Figure 4 illustrates that the median percentage of supine sleep quickly decreases from 21% at baseline to approximately 6% at day 9 (end of training phase), that this percentage of supine sleep further decreases during the therapy phase (starting on day 10) to 2–3%, and that this percentage of supine sleep is maintained over time. This is an interesting finding because the most studied form of PT, the tennis ball technique, has been shown to be minimally effective in the long term, because more than 80% of long-term users either do not use it or avoid the supine position while asleep during tennis ball therapy.[14]

Long-term follow-up is important in any study that evaluates treatment with a detachable device, because the device only exerts its effects when in use. CPAP devices currently are equipped with built-in counters to enable assessment of the hours of use. Several studies have shown that 29–83% of CPAP users are noncompliant with therapy (using study periods of 3 months to 1 y), when compliance is defined as at least 4 h of CPAP use per night.[16] Objective usage data for MAD, until recently,[25] have been difficult to collect and limited to subjective self-report. However, the same group of researchers reported on a high correspondence between objective and subjective long-term MAD compliance data.[26] Long-term subjective MAD compliance rates vary greatly between studies and have shown to be from 4% to 82% after 1 y of treatment.[27-30] Long-term PT compliance has been hampered by discomfort and reports on compliance so far have been limited to subjective measurements. One study evaluated the tennis ball technique (TBT) and

used a follow-up questionnaire in 67 patients for whom the TBT was prescribed, with an average follow-up time of 2.5 ± 1.0 y, and found that long-term compliance was less than 10%.[14] Another group studied 14 patients with POSAS for whom a supine sleeping position preventive vest was prescribed, and found subjective compliance at an average time of 24 months to be less than 30%.[31] To our knowledge, only one study has been conducted evaluating objective long-term use of PT. In this study, 16 patients used a somewhat bulky mass placed against the back for a period of 3 months. Using a built-in actigraphic device they found that their device, on average, was used during 73.7% ± 29.3% of nights for 8.0 ± 2.0 h/night.[32] The SPT is equipped with a built-in sensor enabling assessment of hours of use by both physician and patient. Compliance, using CPAP's compliance criteria,[23] was 64.4% in our current study. Self-reported compliance after 6 months of therapy seems to correspond well with the objective compliance rate and was 59.8%. Objective regular SPT use was 71.2%; subjective regular use was 74.4%. The high correspondence between subjective and objective compliance data is in line with a recent study focusing on subjective and objective MAD compliance data.[26] This finding could suggest that patients are relatively accurate in their estimation and report of their mean use of more than 4 h per night. However, correlation between the self-reported and objective data on continuous use could not be calculated because of the differences in structure of the data. The subjective compliance rate was based on a single question at 1, 3, and 6 months in which the mean use per night during the overall preceding period of use was questioned. The objective data on continuous use were measured on a day-to-day basis by the SPT. In addition, increased patient guidance and the use of educational and positive reinforcement programs might be used to even further increase SPT compliance because these tools have been shown to increase CPAP compliance.[33-36] To our knowledge, 64.4% is the second highest long-term compliance rate of any positional therapy device studied so far. Only the study by Heinzer et al.[32] reported on a higher PT compliance rate. However, the shorter study period (3 versus 6 months), the smaller sample size (N = 16 compared to N = 106) and strict inclusion criteria used in that study (prior nontolerance of either CPAP or oral device therapy and a required < 10% of total sleep time spent in supine sleeping position during a test night with the device) might overestimate their reported compliance rate.

There are some limitations concerning our study setup and data that need to be addressed. One hundred forty-five patients were included in our study. Thirty-nine patients did not register their SPT in the online database. No SPT use or SPT data could be retrieved in these patients, despite implementation of protocolled safety nets; registered patients would receive an email reminding them to fill out the questionnaires in case they had not done so in time. When designing this trial, the possibility of patients not registering online was not fully taken into account. SPT instructions and delivery were taken care of by a Dutch medical device distributor company. The process of registering online was left to the patient, which was not ideal from a research perspective in hindsight. However, the results of this study, in terms of follow-up potential, are likely a good reflection of clinical reality. Of these 106 patients, only 53 patients uploaded their SPT data for the full study period and filled in the questionnaires at two or more time points. Patients did not receive any other incentives to fill out the questionnaires or upload their data. The data retrieved over the full 6 months might therefore have resulted in a positive selection bias, showing merely the best SPT users. However, some patients reportedly stopped using the SPT because they felt

better, no longer had any subjective complaints, and learned to avoid sleeping in the supine position. We were not able to collect their experiences in the questionnaires because most of these patients had already stopped using the SPT in the first weeks of use and were therefore lost to follow-up. Any potential learning effect[10] of PT in general or in sleeping with the SPT remains to be investigated.

This study lacks objective measures on treatment efficacy by means of a repeat PSG in all patients to evaluate effects on AHI and snoring. Although effects of SPT use on AHI have been reported before,[7] effects of the SPT on snoring remain to be investigated. Another limitation of our study is the lack of a control group. Our results and conclusions could have been stronger and more valuable had we compared the SPT users to a group of patients with POSAS with another treatment regimen.

A final limitation of the current study was the lack of an educational program or positive reinforcement program for the patients. Loss to follow-up would probably have been less and compliance would probably have been higher given the positive results in trials with CPAP users.[33-36]

It is our opinion that in patients with mild and moderate POSAS, PT could be the ideal method and maybe should be the initial treatment of POSAS. The treatment concept of SPT, which consists of a small apparatus that is able to register body position as well as provide active feedback effectively to its user during both night and day, seems to be the best currently available option for treating patients with POSAS. This cohort of patients with POSAS using the SPT for a 6-month study period has shown that the SPT is capable of quickly reducing the percentage of supine sleep time within 10 days and maintaining this decreased percentage of supine sleep time over time. Furthermore, SPT use diminished subjective sleepiness and improved sleep related quality of life. However, future prospective long-term research is necessary and should focus on objective PSG parameters in direct comparison with other generally accepted treatment modalities as well as objective measurements of continuous usage.

CONCLUSION

Over a period of 6 months, sleeping with the SPT effectively and persistently decreases the percentage of supine sleep time from 21% to 3% within 10 days and maintaining this 3% supine sleep time over 6 months. The SPT significantly diminishes subjective sleepiness and improves sleep related quality of life in patients with mild to moderate POSAS. Of the 106 patients studied, 64.4% using the SPT were considered compliant, defined as SPT use of more than 4 h per night during 7 days/week and 71.2% of patients used the SPT on a regular basis, defined as more than 4 h during 5 days/week. Subjective and objective compliance data corresponded well. Future research needs to focus on objective long-term treatment effects, particularly in relation to other already generally accepted POSAS treatment modalities.

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CHAPTER 6

Exploration of the relationship between sleep position and isolated tongue base or multilevel surgery in obstructive sleep apnea

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ABSTRACT

Study objective

To elucidate the role of sleep position as a confounding factor on apnea hypopnea index (AHI) and surgical success in isolated tongue base or multilevel surgery.

Methods

This study was conducted using retrospective analysis of patients who underwent hyoid suspension because of obstructive sleep apnea syndrome (OSAS), in the St. Lucas Andreas Hospital, Amsterdam, The Netherlands, from 2004 to 2011. Concurrent surgical treatment was documented. Sleep positions and corresponding AHIs before and after surgery were compared.

Results

A total of 130 patients were included. 94 patients underwent surgery of base of tongue and palate (either uvulopalatopharyngoplasty or Z-palatoplasty), of whom 72 underwent concurrent radiofrequent thermotherapy of the base of tongue. 36 patients underwent base of tongue surgery alone, of whom 22 underwent concurrent radiofrequent thermotherapy of the base of tongue. 65 patients either had a successful reduction in AHI or in AI. Isolated tongue base or multilevel surgery was as successful on the supine AHI as it was on the AHI in other sleeping positions. Surgery was not more successful in the group with position-dependent patients as compared with the non-position-dependent patients (P = 0.615). Successful and non-successful surgical results could not be explained by variations in percentages of supine sleep position.

Conclusion

Sleep position is not a confounding factor on surgical outcomes in tongue base surgery. The results of isolated base of tongue or multilevel surgery in position-dependent OSAS patients leave room for improvement, possibly through positional therapy.

INTRODUCTION

Continuous positive airway pressure (CPAP), introduced in 1981 by Sullivan, is in many countries regarded as the gold standard in treatment of OSAS, with oral device therapy (mandibular reposition appliance, MRA) or surgery in reserve for CPAP failures.[1] Unfortunately CPAP compliance rates are often poor. Weaver and Grunstein report in their review that 29-83% of patients are non-adherent and use their CPAP less than 4 hours per night.[2]

Since treatment remains indicated in patients with severe OSAS with CPAP failure, treatment alternatives are being explored. A variety of site-specific surgical techniques have been developed. The traditional uvulopalatopharyngoplasty (UPPP) or Z-palatopharyngoplasty (ZPP) can be applied in patients with a palatal obstruction.[3] In patients with a base of tongue obstruction site, hyoidthyroidpexia (HTP), radiofrequent ablation of the base of tongue or genioglossus advancement (GA) for example, can be considered.

Traditionally, both subjective (quality of life, Epworth sleepiness scales, etc) and objective outcomes (polysomnography (PSG) variables) of surgical success are reported in literature. Success rates of isolated tongue base surgery and of multilevel surgery have been extensively reported and vary between 40 and 62%, depending on variables such as baseline AHI, BMI, level and configuration of obstruction and on the definition of success used.[4-9] Various PSG parameters such as the AHI or desaturation index (DI), are commonly reported but rarely attention is paid to the distribution of the variables (AHI for example) in the 4 sleeping positions, namely the supine, left, right and prone sleep position.

An increasing amount of literature is being published on the role of sleep position in OSAS.[10-24] Cartwright was the first to define the current positional OSAS (POSAS) criteria: an AHI in the worst sleeping position twice or more as compared to the AHI in the other positions.[12] In two studies from Israel and the Netherlands a remarkable steady 56% of patients have POSAS.[18,19,21] An additional 30% of patients have a higher AHI in supine position than in the other positions, but not twice as high.

As early as 1978, Harper and Sauerland suggested that when sleep apnea patients sleep in supine position, the tongue tends to fall backward against the pharyngeal wall, due to gravity.[25] Our group recently reported that base of tongue obstruction or epiglottis obstruction, albeit not statistically significant, is associated with POSAS.[26] We therefore question whether sleeping position may play a role in poorly understood successes and failures in sleep surgery; tongue base surgery in particular. We aimed to elucidate the role of sleep position as a confounding factor on AHI and surgical success in tongue base surgery.[27]

The aims of this study were as follows:

1. Were unexplained positive or negative outcomes related to variations in percentages of supine sleep position?
2. What was the effect of tongue base surgery on the AHI in supine position in comparison to other sleep positions?
3. Is positional OSAS a predictor of surgical outcome?

MATERIALS AND METHODS

Patients

We retrospectively reviewed our institutional database of patients diagnosed with OSAS and treated with sleep surgery in our hospital from 2004 to 2011. The diagnostic work-up consisted of patient history, physical examination, a full overnight PSG and midazolam or propofol induced sleep endoscopy to evaluate the site(s) of obstruction and further treatment. In this period (2004-2011) patients were operated on by different surgeons, but all surgical procedures were supervised by one and the same surgeon and thus performed the same way. Patients with moderate to severe OSAS and both retrolingual and retropalatal collapse and refusal or non-acceptance of CPAP treatment were offered multilevel surgical treatment.

In this study we retrospectively included patients with moderate to severe OSAS who had undergone a hyoid suspension[28] with or without additional surgical treatment: an uvulopalatopharyngoplasty according to Fujita[29] (in patients with tonsils) or Z-palatoplasty according to Friedman[30] in patients without tonsils and radiofrequent ablation of the base of tongue (RFTB).[31]

Polysomnography

Polysomnogram recordings were carried out using a digital polygraph system (Embla A10, Broomfield, USA). This recorded 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 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. Data were downloaded to the computer and analysed by dedicated sleep software (Somnologica, Broomfield, USA) and manually reviewed for analysis by an experienced sleep investigator.

Definitions

The recommended diagnostic criteria for obstructive sleep apnea syndrome included an apnea hypopnea index (AHI) of 5 or more and evidence of daytime sleepiness. The AHI was defined as the mean number of apneas and hypopneas per hour during sleep, an apnea as a period of 10 seconds or more with a reduction of oronasal airflow of > 90 %. A hypopnea was defined as an episode of more than 30% airflow reduction of the baseline (calculated from the preceding period of 100 seconds) during at least 10 seconds. As per the AASM guidelines AHI thresholds were 5, 15 and 30 events per hour for mild, moderate and severe levels of OSAS, respectively.[32] Desaturation index was defined as the number of desaturations ≥ 4% for a minimum of 10 seconds per hour of sleep. Full overnight PSG was repeated 3 to 4 months postoperatively. Surgical success was defined according to Sher's criteria: AHI reduction of at least 50% and AHI reduction to below 20.[33] When using the AI as an outcome measure the following criteria were applied to define success: reduction by at least 50% and below a value of 10.

Statistics

Changes in parameters before and after treatment were tested with a paired Wilcoxon signed rank test. Differences between groups were tested with a χ^2-test in case of categorical variables and with a Wilcoxon rank sum test in case of continuous variables. The influence of treatment on POSAS was tested with the McNemar test for matched pairs. Exact 95% confidence intervals were calculated for the success proportions and the (overall) response rates. All statistical analyses were performed with SPSS (version 15.0). A p-value < 0.05 was considered to be significant.

RESULTS

We included 130 patients; patient characteristics are shown in table 1. Ninety-four patients underwent a combined procedure of base of tongue and palate, from which 72 underwent concurrent radiofrequent thermotherapy of the base of tongue (RFTB). Thirty-six patients underwent base of tongue surgery alone (HTP), from which 22 underwent concurrent RFTB.

No significant differences in AHI, supine AHI, non-supine AHI, percentage of supine sleep position, total sleep time, arousal index and awakenings were found between the different surgical groups when divided into solely base of tongue surgery (HTP either with or without concurrent RFTB) and combined base of tongue and palate surgery (with either UPPP or ZPP) (table 2).

The mean AHI of all 130 patients decreased significantly from 36.7 to 25.1 (P<0.001). AHI in supine position decreased significantly from 51.2 to 39.3 (P<0.001). AHI in left position decreased significantly from 23.7 to 11.2 (P<0.001). AHI in right position decreased significantly from 21.1 to 14.2 (P<0.001). AHI in prone position decreased significantly from 11.2 to 6.4 (P<0.001).

A successful reduction in AHI, according to Sher's criteria was seen in 49 patients (CI: 29.3-46.6%) and in AI in 54 patients (CI: 33.2-50.9%). Half of the patients (CI: 41.1-58.9%) either had a successful reduction in AHI or in AI.

Table 1 - Baseline characteristics.

Variable	mean ± SD
Age (year)	49.9 ± 9.7
BMI (kg/m^2)	27.3 ± 2.8
AHI (/h)	36.7 ± 14.4
AHI supine (/h)	51.2 ± 24.8
% AHI supine	37.4 ± 24.7
ratio male:female	9:1

SD=standard deviation.

Table 2 - Mean values of AHI and AHI in different positions, before and after surgery for different groups of patients. Boldfaced values are the significant differences before and after treatment within the groups or between the groups.

	mean (before)	mean (after)	P-value (within)	mean (before)	mean (after)	P-value (within)	P-value (between)
AHI successful*:		yes (n=49)			no (n=81)		
AHI	35.8	9.5	**<0.001**	37.2	34.5	0.099	**<0.001**
AHI supine	49.1	18.9	**<0.001**	52.5	51.6	0.749	**<0.001**
AHI non supine	23.1	5.1	**<0.001**	27.7	23.9	0.052	**<0.001**
AHI prone	4.9	3.5	0.647	15.0	8.1	**0.033**	0.234
AHI left	18.7	4.9	**<0.001**	26.8	20.3	**0.004**	0.077
AHI right	15.9	4.8	**<0.001**	24.2	19.9	0.137	0.061
% supine sleep position	42.8	36.9	0.126	34.2	37.9	0.124	**0.024**
AI successful#:		yes (n=54)			no (n=76)		
AI	20.0	2.7	**<0.001**	21.0	21.9	0.376	**<0.001**
AHI	34.4	13.1	**<0.001**	38.3	33.9	**0.026**	**<0.001**
AHI supine	51.8	24.1	**<0.001**	51.5	50.5	0.792	**<0.001**
AHI non supine	22.7	8.7	**<0.001**	28.2	22.8	**0.011**	**0.003**
AHI prone	10.4	3.4	0.154	11.9	8.5	0.161	0.922
AHI left	21.9	8.3	**<0.001**	25.4	19.1	**0.006**	**0.029**
AHI right	18.5	7.5	**0.001**	23.3	19.2	0.098	0.141
% supine sleep position	36.8	37.7	0.679	38.4	37.7	0.886	0.720
AHI or AI successful:		yes (n=65)			no (n=65)		
AHI	34.8	13.1	**<0.001**	38.5	37.1	0.501	**<0.001**
AHI supine	49.8	23.8	**<0.001**	52.7	54.8	0.498	**<0.001**
AHI non supine	23.6	8.4	**<0.001**	28.3	25.2	0.152	**<0.001**

AHI prone	9.4	3.5	0.115	12.9	9.2	0.197	0.808
AHI left	20.8	8.2	**<0.001**	26.7	20.9	**0.023**	**0.027**
AHI right	18.0	6.9	**<0.001**	24.2	21.4	0.258	0.071
% supine sleep position	38.2	37.2	0.838	36.7	37.9	0.575	0.565
positional OSAS[†]:		yes (n=70)			no (n=60)		
AHI	32.7	23.7	**<0.001**	41.3	26.6	**<0.001**	**0.044**
AHI supine	57.9	42.2	**<0.001**	43.5	35.6	0.132	0.107
AHI non supine	14.9	13.3	0.106	38.8	20.8	**<0.001**	**<0.001**
AHI prone	4.4	6.3	0.793	19.1	6.4	**0.002**	**0.039**
AHI left	16.0	11.6	0.159	32.8	17.9	**<0.001**	**<0.001**
AHI right	12.8	13.0	0.501	30.8	15.6	**<0.001**	**0.001**
% supine sleep position	43.9	43.9	0.654	29.9	30.1	0.853	0.642
treatment		HTP/HTP+RFTB (n=36)			HTP+UPPP/ZPP (n=94)		
AHI	26.7	16.4	**<0.001**	38.4	26.5	**<0.001**	0.744
AHI supine	41.4	30.4	0.059	52.9	40.7	**<0.001**	0.837
AHI non supine	19.8	8.5	**0.001**	27.0	18.2	**<0.001**	0.676
AHI prone	9.6	0.5	**0.043**	11.4	7.4	0.133	0.275
AHI left	15.5	10.8	0.055	25.2	15.2	**<0.001**	0.474
AHI right	19.0	8.5	**0.010**	21.5	15.1	**0.008**	0.365
% supine sleep position	34.2	42.1	0.260	38.0	36.8	0.750	0.162

[*]: Reduction in AHI of at least 50% and to below 20.
[#]: Reduction in AI of at least 50% and to below 10.
[†]: AHI supine/AHI non supine > 2.

In general, patients who had a successful reduction in AHI slept less often in supine position after treatment than before treatment compared to the patients who did not have a successful reduction in AHI (P=0.024). The difference between the percentage of total sleep time (TST) in supine position before and after surgery was not significant within each group (P=0.126 and P=0.124 for both groups respectively). The mean difference in AHI before and after treatment was 26.3/h in the group of patients with a successful reduction in AHI, which is significantly higher than the mean difference in the other group (P<0.001). The mean AHI in supine position decreased by 30.2/h in the first group, again significantly higher than the difference in the other group (P<0.001). The differences in AHI, AHI in supine position and AHI in non-supine position before and after treatment were all significant for the patients with successful AHI reduction (all P<0.001), and not for the patients in the non-successful group (P=0.099 total AHI, P=0.749 AHI supine, P=0.052 AHI non supine). The AHI in left or right position decreased significantly for the successful group, AHI in prone position did not. In the unsuccessfully treated group, the AHI in prone and left position did decrease significantly after surgery (table 2). Total sleep time, arousal index and number of awakenings did not change significantly after surgery (data not shown here).

Seventy patients suffered from POSAS pre-operatively. Within this group the total AHI decreased significantly from 32.7 to 23.7 (P<0.001), the AHI in supine position decreased significantly from 57.9 to 42.2 (P<0.001). The percentage slept in supine position did not change significantly after treatment (P=0.654). In 34 of the 70 position-dependent patients the treatment was successful (CI 36.4-60.1 %) (table 3). The other 60 pre-operative non-POSAS patients had a significantly lower AHI following surgery (P<0.001). A significant decrease of the AHI was seen in all positions except the AHI in supine position. The difference in supine AHI before and after treatment between the POSAS and non-POSAS groups was not significant (P=0.107), while the AHI decreased more for the non-POSAS patients (P=0.044) (table 2). Furthermore, in the non-POSAS patients the post-operative decrease in non-supine, prone, left and right AHI was significant when compared to these parameters in the POSAS patients (P<0.001, P=0.039, P<0.001, P=0.001).

Surgery was not more successful in the group with position-dependent patients than in the other group (P=0.615) (figure 1). Most positional patients remained positional after surgery and most non-positional patients remained non-positional (72.9% and 57.6%, P=0.451) (table 4).

Table 3 - Success rates split for different outcomes of positional OSAS. The p-values denote the difference in these rates between the two groups.

	Percentage	95% CI	Percentage	95% CI	P-value
positional OSAS*:	**yes (n=70)**		**no (n=60)**		
AHI successful	35.7%	24.6 - 48.1%	40.0%	27.6 - 53.5%	0.615
AI successful	42.9%	31.1 - 55.3%	40.7%	28.1 - 54.3%	0.803
AHI or AI successful	48.6%	36.4 - 60.1%	51.7%	38.4 - 64.7%	0.725

*: AHI supine/AHI non supine > 2. CI=confidence interval.

Table 4 - Effect of surgery on position-dependency.

Positional OSAS*		**Post treatment**				
		No		**Yes**		
		N	**%**	**N**	**%**	**P-value**
Pre treatment	**No**	34	57.6%	25	42.4%	0.451
	Yes	19	27.1%	51	72.9%	

*: AHI supine/AHI non supine > 2.

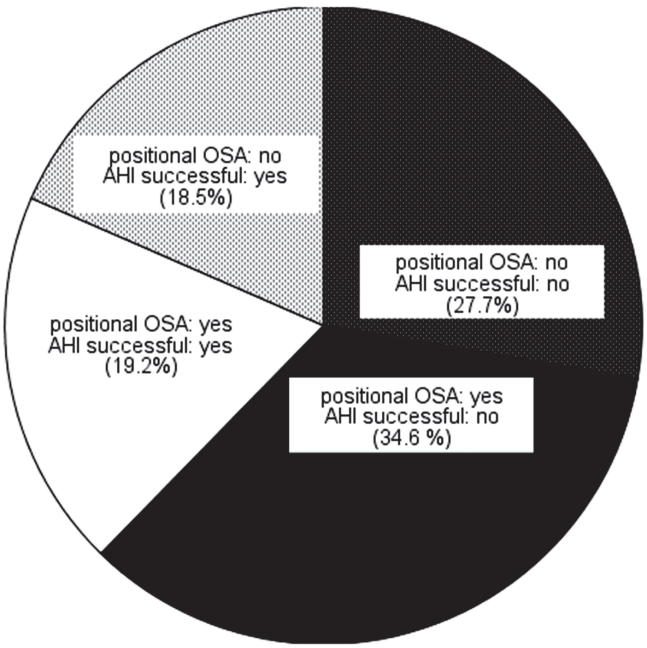

Figure 1 - Distribution of surgical success amongst POSAS and non-POSAS patients.

DISCUSSION

The present study is the first which looks into the relation between tongue base surgery either with or without concurrent palate surgery and sleep position.

Our study population did not solely consist of isolated base of tongue surgery patients but also included patients who concurrently underwent palate surgery. Ideally we would have studied isolated base of tongue surgery. But most patients we diagnostically worked up for HTP suffered from multilevel obstruction. Although we compared the isolated base of tongue surgery group to the combined base of tongue and palate surgery group and found no significant differences between the groups this is a limitation of our study.

To our best knowledge only three earlier studies have been published on the effect of sleep position on outcomes of palate surgery (UPPP).[27,34,35] So far, no papers have been published on the combination approach of sleep surgery and positional therapy (PT). The overall success rate and overall response rate of this series of HTP/tongue base surgery with or without concomitant palatal surgery in patients with moderate to severe OSAS and CPAP failure are 38% and 60% respectively, which is in the low-normal range compared to previously reported series.[4-9] Improvement of treatment outcome is mandatory if treatment intent is “salvage” in CPAP failures.

It is a clinical reality in sleep surgery that remarkable differences in outcome can occur amongst patients with comparable pre-operative AHI, BMI, clinical findings such as tongue size, tonsil size and drug induced sleep endoscopy (DISE) findings.[26,35] We took a closer look to evaluate whether discrepancies between expected and actual outcome could be explained by changes in body position before and after treatment. For this reason the patients in the present series were divided into a positional and non-positional group. In general, in both positional and non-positional patients, the percentage supine sleep position remained remarkably constant after surgery and remarkable successes or failures could not be explained by considerable changes in percentage supine position. In conclusion, surgery did not influence patient’s position-dependency (table 4).

Hyoid suspension is traditionally thought to exert its effect by increasing the retrolingual airway space. We hypothesised therefore that in successful surgery more outspoken decreases in AHI would be found in the supine position, than in other sleep positions. Our results show that HTP did not have better effect on the supine AHI in comparison to the AHI in other sleeping position components. When surgery was either successful or non-successful, the reduction in AHI was uniform in all sleeping positions. Earlier Stuck et al. reported that MRI studies do not show enlargement of the retrolingual airway space following HTP. These authors concluded that the effect of HTP was in increased general stabilization of the upper airway, not an enlargement of the retrolingual airway.[36] Our present findings provide further support for this concept. However, our follow-up was relatively short (3-4 months). Further research, to evaluate long term results is ongoing.

POSAS occurs in 56%[21] of OSAS patients. PT as treatment for POSAS is gaining momentum.[24] After surgical failure in positional patients, a further decrease of the AHI can theoretically be accomplished by prevention of the supine sleep position. This leads to the concept of multimodality treatment. Theoretically, in POSAS, multilevel surgery with PT would achieve better results than surgery or PT alone. This is in concordance with earlier research papers in palate surgery. Katsantonis et al. studied the effect of UPPP on sleep posture and differences in uvulopalatopharyngoplasty (UPPP) results in various sleep positions in a small series of 17 patients.[34] They found that following UPPP, the AHI significantly improved in the lateral position. They also found that during sleep in a supine position, the AHI did not show significant improvement. They conclude that UPPP enhances the position effect on OSAS because it readily eliminates obstructive events in the lateral sleep position. In other words the difference in AHI in supine and non-supine positions are more pronounced postoperatively. They are of opinion that additional positional therapy could significantly improve response to treatment with UPPP. Lee et al. studied the effect of sleep position on surgical outcomes as well.[27] They studied 69 consecutive patients who underwent a UPPP. After categorizing the patients into four groups according to the change in AHI after surgery, they found that the failure group had a higher proportion of supine position dependency than any other group. In a second paper published by the same group, results show that UPPP is a successful treatment for obstructive events occurring in the lateral sleep position, especially in patients without positional dependency.[37] The suggestion is made that patients who have become position-dependent may benefit from positional therapy after UPPP.

Until recently, PT consisted of the “tennis ball technique”. A variety of tennis balls, squash balls, shark fins, special pyjamas and vests all had the same concept of a bulky mass worn on the back. All these devices have in common that they are not comfortable, disrupt sleep architecture and the long term compliance is a disappointing 10%.[38] A recent paper by our group for the first time showed that a small buzzing device worn in the neck can prevent supine sleeping position without disrupting sleep.[24]

CONCLUSION

The difference between the percentage of total sleep time in supine position before and after surgery was not significant. The differences in AHI, AHI in supine position and AHI in non-supine position before and after treatment were all significant for the patients with successful AHI reduction (all P<0.001), and not for the patients in the non-successful group (P=0.099 total AHI, P=0.749 AHI supine, P=0.052 AHI non supine). Isolated tongue base or multilevel surgery was as successful on the supine AHI as it was on the AHI in other sleeping positions.

Surgery was not more successful in the group with position-dependent patients as compared to the non-position-dependent patients (P=0.615). Successful and non-successful surgical results could not be explained by variations in percentages of supine sleep position. Surgery was not more successful in the group with position-dependent patients than in the non-position-dependent group (P=0.615). From this retrospective analysis we conclude that sleep position is not a confounding factor on surgical outcomes in tongue base surgery. The results of base of tongue or multilevel surgery in position-dependent OSAS patients leave room for improvement, possibly through positional therapy. Further research on the combined effect of multilevel surgery and positional therapy is ongoing.

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CHAPTER 7

Theoretical approach towards increasing effectiveness of palatal surgery in obstructive sleep apnea: role for concomitant positional therapy?

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ABSTRACT

Study objective

Evaluate the effect of palatal surgery (uvulopalatopharyngoplasty (UPPP) or Z-palatoplasty (ZPP)) with or without (+/-) concomitant radiofrequent ablation of the base of tongue (RFTB) on body position specific apnea hypopnea index (AHI) values in patients with obstructive sleep apnea (OSAS). Compare this treatment outcome to the theoretical effect of (addition of) positional therapy (PT).

Methods

Retrospective analysis of pre and posttreatment polysomnographies in 139 patients who had undergone UPPP/ZPP +/- RFTB. Hypothetical evaluation of the effects of (addition of) ideal PT on AHI in positional OSAS (POSAS) patients.

Results

Median AHI significantly decreased from 18.0 to 11.2 ($p<0.001$). Median AHI in all separate positions decreased significantly as well. Sixty-eight patients suffered from POSAS and showed a significant decrease in median AHI from 15.5 to 11.5 ($p=0.002$). In the 71 non-positional OSAS (NPOSAS) patients the significant AHI decrease was more outspoken, from 23.0 to 11.0 ($p<0.001$). Our hypothetical model to treat POSAS patients with an ideal PT (as monotherapy or in addition to surgery) resulted in a significant median AHI decrease from 18.0 to 4.5 ($p<0.0001$).

Conclusion

UPPP/ZPP +/- RFTB significantly reduces AHI and all body position specific AHI values. This reduction is significantly higher in NPOSAS than in POSAS patients. When considering UPPP/ZPP +/- RFTB, effect of body position needs to be taken into account. PT, either as monotherapy or in addition to surgery, theoretically has shown to improve treatment results dramatically in POSAS patients. Prospective, controlled trials focusing on the effects of this combination of treatments should further evaluate this hypothetical conclusion.

INTRODUCTION

Continuous positive airway pressure (CPAP) is regarded as gold standard in patients with (moderate and severe) OSAS.[1] However, CPAP suffers from compliance problems causing the gold standard to be suboptimal.[2]

Alternative treatment options for OSAS are conservative measures (e.g. weight reduction, abstinence from alcohol and sedatives), positional therapy,[3] oral device therapy[4] and surgery. A Cochrane review does not recommend surgery at all for OSAS, except in studies.[5] However, it is in concordance with clinical experience that adherence to CPAP, when defined as greater than 4 hours of nightly use, is between 17 and 54%,[6] resulting in a significant number of patients abandoning CPAP and seeking alternative treatments, such as oral appliances and surgery. Oral appliances also require sufficient compliance, and roughly one third of patients have contraindications to oral devices.[7] In sum, many patients opt for surgical therapy. Uvulopalatopharyngoplasty including tonsillectomy (UPPP) was and probably still is the most commonly performed OSAS surgery worldwide.[8] Surgical success rates of UPPP range from 30-50%.[9,10] A variation of the technique, Z-palatoplasty (ZPP), for patients who had undergone tonsillectomy earlier has been described and has similar outcomes.[11,12] Furthermore, it has been shown that UPPP as single treatment[13,14] or as part of multilevel surgery[15] may be useful to lower CPAP pressure requirements, thereby improving CPAP compliance in selected patients. An increasing amount of literature has been published on the role of sleep position in OSAS and positional therapy.[16-32] Cartwright was the first to define the current positional OSAS (POSAS) criteria: an AHI in the worst sleeping position twice or more as high when compared to the AHI in the other positions.[20] It is evident that the overall AHI is affected by the relative proportion of each of the different sleeping positions. However, the effect of UPPP on body position specific AHI's is not well known. Aims of our current study were to investigate the effect of UPPP and ZPP on body position specific AHI values, investigate the efficacy of UPPP/ZPP for both POSAS and non-positional OSAS (NPOSAS) patients and hypothesize about a possible role for positional therapy to increase treatment efficacy.

MATERIALS AND METHODS

Patients

We retrospectively reviewed our institutional database for OSAS patients treated with sleep surgery from 2004 to 2011. Our institution's general evaluation of patients with sleep disordered breathing consists of the following: patient history, physical examination, polysomnography (PSG) and drug induced sleep endoscopy. Patients were operated on by different surgeons, but all surgical procedures were supervised by the same surgeon and performed in the same way. Patients with mild to severe OSAS and isolated retropalatal collapse or multi-level collapse (retropalatal collapse combined with retrolingual collapse) and refusal or non-acceptance of CPAP treatment were offered surgical treatment. We included patients with mild to severe OSAS who had undergone UPPP according to Fujita[8] (in patients with tonsils) or Z-palatoplasty according to Friedman (ZPP[12]) in patients without tonsils with or without concomitant radiofrequent ablation of the base of tongue (RFTB[33]) in case of a partial retrolingual collapse. Patients, whose two full overnight PSGs could not be retrieved, or whose date of polysomnography was more than 4 months before or 4 months after surgery, or who used other OSAS treatment modalities between the two polysomnographies were excluded from analysis. The study was reviewed and approved by the local human research ethics review board.

Polysomnography

PSG recordings were carried out using a digital polygraph system (Embla A10, Broomfield, USA). This recorded 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 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. Data were downloaded to the computer and analysed by dedicated sleep software (Somnologica, Broomfield, USA) and manually reviewed for analysis by an experienced sleep investigator.

Definitions

The criteria for OSAS included an apnea hypopnea index (AHI) of 5 or more and evidence of daytime sleepiness. The AHI was defined as the mean number of apneas and hypopneas per hour during sleep, an apnea as a period of 10 seconds or more with a reduction of oronasal airflow of > 90 %. A hypopnea was defined as an episode of more than 30% airflow reduction of the baseline (calculated from the preceding period of 100 seconds) during at least 10 seconds. AHI thresholds were 5, 15 and 30 events per hour for mild, moderate and severe levels of OSAS, respectively.[34] Positional OSAS (POSAS) was defined as an AHI ≥ 5 and an AHI in supine position twice or more as high when compared to each of the AHI values found in the other positions.[20] Full overnight PSG was repeated 3 to 4 months postoperatively. Surgical success was defined according to Sher's

criteria: AHI reduction of at least 50% and AHI reduction to below 20.[35] Cure rate was defined as AHI reduction below 5.

Theoretical model using an ideal form of positional therapy (ideal PT) (Figure 1)

Using patients' polysomnographical data a theoretical model to treat patients was applied. Patients were considered POSAS patient and suitable for ideal PT when suffering from a mild to moderate OSAS, sleeping in supine position between 10 and 90% of total sleep time[32] and showing an AHI in supine position twice or more as high when compared to each of the AHI values found in the other positions. Nonpositional patients would receive surgery (UPPP/ZPP +/-RFTB). POSAS patients would start using ideal PT. Ideal PT would reduce the baseline AHI to the baseline non supine AHI. Additional treatment was considered necessary when the posttreatment AHI exceeded 5. Results in terms of changes in AHI, overall success and cure rates of this theoretical model were evaluated.

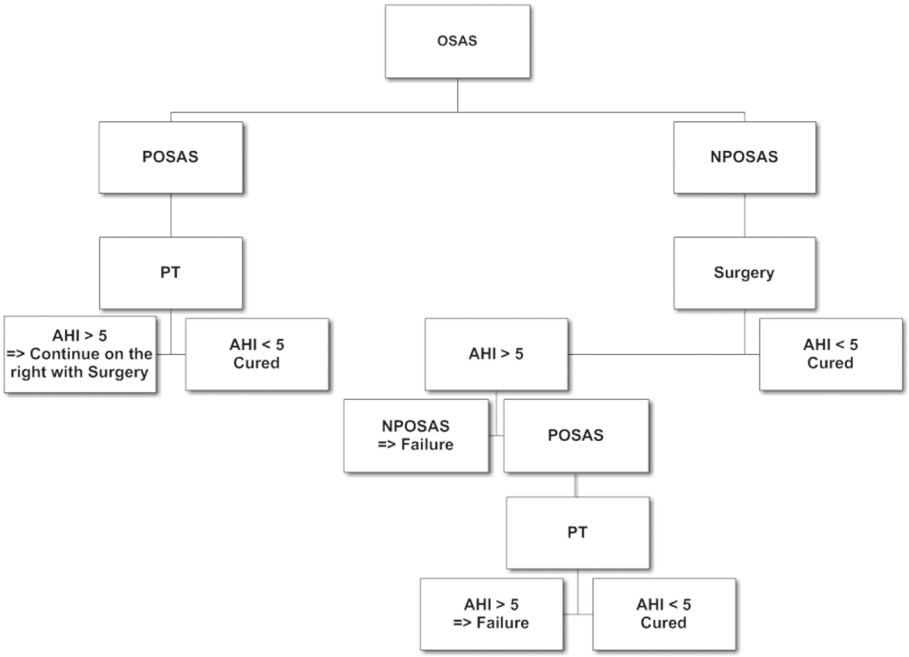

Figure 1 - Flowchart using a theoretical model and an ideal form of PT in OSAS patients. A patient was considered to suffer from POSAS if 5≤AHI≤30 and 10≤ percentage of supine sleep time≤90. Surgery would be the surgical procedure the patient had undergone. OSAS=obstructive sleep apnea, POSAS=positional OSAS, NPOSAS=non-positional OSAS, AHI=apnea hypopnea index, PT=hypothetical ideal positional therapy defined as a reduction of supine time to 0, thereby reducing the AHI to the non-supine AHI.

Statistical analysis

Changes in parameters before and after treatment were tested with the Wilcoxon signed rank test (continuous variables) or with the McNemar test (dichotomous variables). Differences between groups were tested with the Mann-Whitney test or the Kurskal-Wallis test in case of continuous variables and with a χ2-test in case of categorical variables. Exact 95% confidence intervals were calculated for the success rates. All statistical analyses were performed with SPSS (version 20). A p-value < 0.05 was considered to be significant.

RESULTS

We included 139 patients; baseline patient characteristics are shown in table 1. Fifty-two patients suffered from mild, 62 from moderate and 25 from severe OSAS. Fifty-nine patients were treated with UPPP (mild OSAS 21, moderate 25, severe 13), 59 patients with UPPP+RFTB (mild OSAS 23, moderate 26, severe 10) and 21 patients with ZPP+RFTB (mild OSAS 8, moderate 11, severe 2). Fifty-five patients (39.6%) had a successful reduction in AHI, according to Sher's criteria.[35] Twenty-seven out of 139 patients had a postoperative AHI<5 (19.4%). The median AHI of all 139 patients significantly decreased from 18.0 [range: 5.1 – 69.6] to 11.2 [1.0 – 63.0] (p<0.001). The median AHI in all separate positions decreased significantly as well. Number of awakenings, total sleep time, and the percentages of total sleep time slept in supine, left and prone position did not change significantly after treatment (table 2).

Table 1 - Baseline patient characteristics (n=139).

Variable	median [range]
Age (years)	45.0 [25.0 - 69.0]
BMI (kg/m2)	27.4 [20.4 - 38.2]
AHI (/h)	18.0 [5.1 - 69.6]
AHI supine (/h)	30.2 [0.0 - 133.1]
% supine	34.1 [0.0 - 100.0]
Ratio male:female	127:12

Table 2 - Median polysomnographical parameters with interquartile range before and after surgery (n=139).

	before		**after**		
	median	IQR	median	IQR	**P-value**
AHI (/h)	18.0	12.0 - 27.0	11.2	5.6 - 20.2	**<0.001**
AHI supine (/h)	30.2	19.1 - 49.5	20.5	8.3 - 39.9	**<0.001**
AHI left (/h)	8.1	0.4 - 17.8	3.1	0.0 - 11.6	**0.004**
AHI right (/h)	4.4	0.0 - 17.5	2.6	0.0 - 7.6	**0.008**
AHI prone (/h)	0.0	0.0 - 11.1	0.0	0.0 - 0.9	**0.024**
AHI REM (/h)	21.4	11.3 - 33.5	12.8	4.9 - 21.9	**<0.001**
% supine	34.1	17.9 - 56.4	33.1	20.0 - 51.1	0.388
% left	24.1	6.2 - 41.2	29.7	11.0 - 41.7	0.389
% right	22.5	5.3 - 37.0	31.8	9.7 - 42.4	**0.013**
% prone	0.0	0.0 - 7.6	0.0	0.0 - 3.9	0.382
Total sleep time (minutes)	418.2	362.5 - 466.0	424.0	373.5 - 469.0	0.861
Desaturation index (/h)	5.7	2.1 – 12.7	3.8	1.4 – 9.4	**0.001**
Number of awakenings	4.0	2.0 - 6.0	4.0	2.0 - 7.0	0.499
Number of position changes	31.0	21.0 - 55.8	25.0	15.5 - 46.0	**0.022**
Positional change index (/h)	4.5	3.0 - 9.0	4.0	2.0 - 6.0	**0.010**

Boldfaced values represent significant differences. IQR=interquartile range.

Treatment

No significant difference between the treatments was found in the number of patients with a successfully reduced AHI; in 27 patients treated with UPPP (CI: 32.7-59.2%), in 21 patients treated with UPPP+RFTB (CI: 23.6-49.1%) and in 7 patients treated with ZPP+RFTB (CI: 14.6-57.0%) (p=0.432) treatment was found to be successful. Data of patients treated with either UPPP+RFTB or ZPP+RFTB were pooled in one group (n=80) and compared to the patients who underwent UPPP (n=59). Between these groups only the percentage in supine position (increase in UPPP group, decrease in the other group) showed a significant difference between groups (table 3).

Positional OSAS (table 4)

In the 68 patients (48.9%) with POSAS pretreatment AHI decreased significantly from 15.5 [5.1 – 46.5] to 11.5 [1.0 – 40.0] (p=0.002), and AHI in supine position decreased significantly from 33.9 [5.1 – 93.9] to 20.9 [0.0 – 69.5] (p<0.001). No significant decrease was found in the other positions, total sleep time, percentage slept in supine position or number of awakenings. In the 71 NPOSAS patients pretreatment AHI decreased significantly, from 23.0 [5.1 – 69.5] to 11.0 [1.0 – 63.0] (p<0.001). This difference is significantly higher than the difference in the POSAS group (p=0.026). AHI in prone, left and right position decreased significantly more in the NPOSAS group than in the POSAS group (p=0.002, p=0.012 and p=0.005 respectively). No difference was found in the number of patients with a successful reduction of the AHI in both groups: 24 of the 68 patients (35.3%, CI: 24.1-47.8%) suffering from POSAS versus 31 of the 71 patients (43.7%, CI: 31.9-

56.0%) suffering from NPOSAS (p=0.313). Half of the positional patients remained positional after treatment and more than half of the NPOSAS patients remained non-positional after treatment (50.0 and 62.0%, p= 0.443).

Results of the theoretical treatment flowchart

Fifteen of 68 pretreatment POSAS patients were not eligible for ideal PT (4 patients had an AHI > 30, six patients a supine sleep < 10%, five patients > 90%). Thirty-two of these 53 patients would have an ideal PT posttreatment AHI < 5. Two patients in the pretreatment POSAS group were not eligible for ideal PT but showed a posttreatment AHI < 5 following surgery as initial treatment. Three patients would be cured when, following a non-curative (AHI > 5 posttreatment) trial of ideal PT, surgery would be performed. Five patients (who were not eligible for initial ideal PT treatment) would be cured from their OSAS following surgery and additional ideal PT postoperative. Seven patients would ultimately be cured following a non-curative trial of ideal PT, non-curative surgery and ideal PT. In total 49 patients (72.1%) were cured from their OSAS. Their median AHI decreased significantly from 13.7 [5.1 – 34] to 2.5 [0.0 – 4.9] (p<0.0001). For the pretreatment POSAS patients who were not cured (n=19) by this protocol median AHI decreased from 21.5 [11.5 – 46.5] to 10.6 [5.2 – 47.7] (p=0.117). Twelve of 71 NPOSAS patients were cured by surgery alone. Eighteen of 25 pretreatment NPOSAS but posttreatment POSAS patients were eligible for additional ideal PT. Thirteen patients could be cured by combined therapy. By using this treatment protocol 25 out of 71 patients (35.2%) could be cured from their OSAS. Their median AHI decreased significantly from 16.0 [5.1 – 57.2] to 2.1 [0.0 – 4.9] (p<0.0001). The other 46 non-curatively treated NPOSAS patients showed a significant decrease in median AHI from 24.5 [8.0 – 69.6] to 13.1 [5.1 – 63.4] (p=0.001).

Overall this treatment regimen would result in a significant decrease in median AHI from 18.0 [5.1 – 69.6] to 4.5 [0.0 – 63.4] (p<0.0001). Ninety-nine patients (71.2%) would have had a successful reduction in AHI according to Sher's criteria, 74 patients (53.2%) would have been 'cured' from their OSAS based on AHI<5.

Table 3 - Median polysomnographical parameters with IQR before and after palatal surgery with or without concurrent radiofrequent ablation of the base of tongue.

treatment:	UPPP (n=59)					UPPP/ZPP+RFTB (n=80)					
	before		**after**		**P-value**	**before**		**after**		**P-value**	**P-value**
	median	IQR	median	IQR	**(within)**	median	IQR	median	IQR	**(within)**	**(between)**
AHI (/h)	19.0	12.0 - 27.0	9.0	5.0 - 15.0	**<0.001**	17.7	12.1 - 25.1	12.7	6.8 - 24.4	**0.002**	0.069
AHI supine (/h)	30.6	13.8 - 50.7	13.7	6.4 - 34.8	**<0.001**	30.1	21.1 - 49.3	27.2	9.3 - 40.5	**0.006**	0.565
AHI left (/h)	8.2	0.0 - 18.9	2.7	0.0 - 12.1	**0.005**	6.8	1.1 - 15.2	3.3	0.2 - 11.3	0.193	0.199
AHI right (/h)	5.1	0.0 - 18.0	1.4	0.0 - 5.6	**0.001**	4.1	0.3 - 17.3	4.1	0.4 - 12.7	0.438	0.072
AHI prone (/h)	0.0	0.0 - 16.0	0.0	0.0 - 4.2	**0.018**	0.0	0.0 - 4.7	0.0	0.0 - 0.0	0.462	0.108
AHI REM (/h)	20.9	11.7 - 31.3	10.3	4.7 - 22.5	**<0.001**	21.6	9.7 - 33.8	13.2	6.2 - 21.9	**<0.001**	0.505
% supine	24.7	11.8 - 48.9	33.1	18.4 - 50.9	0.282	37.3	21.9 - 62.7	33.0	20.8 - 51.5	0.066	**0.046**
% left	27.0	0.0 - 42.9	28.9	12.3 - 43.6	0.499	23.4	7.0 - 41.2	30.7	10.8 - 39.7	0.582	0.823
% right	21.5	0.0 - 40.1	31.9	1.7 - 41.4	0.204	22.7	7.9 - 36.2	31.3	14.4 - 43.6	**0.030**	0.792
% prone	3.4	0.0 - 9.3	0.0	0.0 - 7.3	0.104	0.0	0.0 - 5.9	0.0	0.0 - 1.7	0.623	0.087
Total sleep time (minutes)	408.0	354.5 - 459.0	412.5	352.3 - 465.0	0.667	431.5	379.3 - 474.6	436.3	391.1 - 477.3	0.571	0.535
Number of awakenings	3.0	2.0 - 6.0	3.0	2.0 - 7.0	0.742	4.0	2.0 - 6.0	4.0	2.0 - 7.0	0.520	0.922
Number of position changes	27.0	18.0 - 48.5	24.5	15.8 - 47.5	0.517	33.0	21.0 - 58.0	30.0	15.0 - 45.0	**0.015**	0.277
Positional change index (/h)	4.0	2.0 - 8.5	4.0	2.0 - 7.0	0.260	5.0	3.0 - 9.0	4.0	2.0 - 6.0	**0.014**	0.377

Boldfaced values represent significant differences.

Table 4. Median polysomnographical parameters before and after surgery for POSAS and NPOSAS patients.

positional OSAS:	yes (n=68)					no (n=71)					
	before		**after**		**P-value (within)**	**before**		**after**		**P-value (within)**	**P-value (between)**
	median	IQR	median	IQR		median	IQR	median	IQR		
AHI (/h)	15.5	10.9 - 21.7	11.5	5.0 - 21.2	**0.002**	23.0	14.3 - 31.0	11.0	6.1 - 20.1	**<0.001**	**0.026**
AHI supine (/h)	33.9	22.2 - 50.6	20.9	8.4 - 38.3	**<0.001**	27.2	15.0 - 49.5	20.5	7.8 - 42.2	**0.014**	0.168
AHI left (/h)	3.1	0.0 - 9.4	1.9	0.0 - 8.0	0.567	15.1	4.3 - 28.1	4.5	1.2 - 15.6	**0.001**	**0.012**
AHI right (/h)	2.5	0.0 - 5.8	1.7	0.0 - 6.2	0.985	14.1	0.0 - 29.8	4.6	0.0 - 12.8	**0.001**	**0.005**
AHI prone (/h)	0.0	0.0 - 0.0	0.0	0.0 - 0.0	0.438	0.0	0.0 - 23.0	0.0	0.0 - 4.2	**0.003**	**0.002**
AHI REM (/h)	18.6	7.7 - 29.5	12.8	4.4 - 21.9	**0.011**	24.2	12.7 - 38.3	12.6	6.5 - 22.5	**<0.001**	**0.039**
% supine	34.9	18.5 - 56.3	34.5	22.0 - 51.1	0.562	31.6	15.1 - 58.3	29.1	18.6 - 51.6	0.541	0.948
% left	23.0	4.2 - 39.0	27.4	4.3 - 41.6	0.636	27.0	6.9 - 45.6	30.3	16.5 - 42.8	0.497	0.861
% right	22.8	5.5 - 39.8	33.1	11.0 - 43.4	0.107	22.2	5.3 - 35.2	30.4	6.3 - 42.3	**0.049**	0.899
% prone	0.0	0.0 - 5.8	0.0	0.0 - 1.8	1.000	1.8	0.0 - 8.9	0.0	0.0 - 7.3	0.195	0.266
Total sleep time (minutes)	423.0	379.3 - 464.8	421.5	373.1 - 461.3	0.721	416.0	355.0 - 470.1	425.0	374.0 - 478.0	0.538	0.559
Number of awakenings	4.0	1.3 - 7.0	4.0	2.0 - 7.0	0.758	4.0	2.0 - 6.0	3.5	2.0 - 7.0	0.490	0.930
Number of position changes	31.0	20.0 - 53.3	30.5	16.0 - 47.8	0.127	31.0	21.0 - 57.3	25.0	15.0 - 45.0	0.070	0.685
Positional change index (/h)	4.5	3.0 - 7.3	4.0	2.0 - 7.0	0.149	4.5	2.8 - 10.0	4.0	2.0 - 6.0	**0.029**	0.420

Boldfaced values represent significant differences.

DISCUSSION

The present study is the first which extensively looks into the relation between UPPP or ZPP either with or without concomitant radiofrequent ablation of the base of tongue (UPPP/ZPP +/- RFTB) and sleep position PSG parameters. We found better results of UPPP/ZPP +/- RFTB in NPOSAS patients compared to POSAS patients (table 4). Surgery did not enhance the position effect. In contrast, 50% of POSAS patients did not show positional dependency any longer after surgery, whereas only 38% of NPOSAS patients became POSAS patients following surgery. Although it has been shown previously that PSG might overestimate the severity of OSAS in some patients with POSAS because of an increase in time spent supine compared to nights not wearing the PSG apparatus[36] it has also been shown that the correlations between PSG night 1 and 2 for the percentage of time spent supine and the supine AHI are similar and highly significant.[37]

In our study AHI and all sleeping position specific AHI values showed a significant decrease in both the isolated palatal surgery group (table 3) as well as the total patient group (table 2). When studying POSAS and NPOSAS patients we found that in the POSAS patient group AHI showed a significant decrease, which mainly might be due to the significant decrease in AHI supine. In NPOSAS patients the significant AHI decrease might be caused by the significant effect on all body specific AHI values. Since POSAS patients have lower non-supine AHI values compared to NPOSAS patients a larger number of patients might be needed to detect the significant decrease in their non-supine AHI values. Studying table 4 it therefore cannot be concluded that in POSAS patients palatal surgery exerts its effects solely in supine position.

Only three earlier studies analyzed the effect of sleep position on outcomes of (isolated) UPPP.[38-40] Katsantonis et al. studied the effect of UPPP on the sleeping position specific AHI values in 17 patients.[38] They found that following UPPP, the AHI significantly improved in the lateral position and that during sleep in supine position, the AHI did not show significant improvement. They concluded that UPPP enhances the position effect on OSAS because it eliminates obstructive events in the lateral sleep position. Although our study also comprises of patients who underwent RFTB both the UPPP and UPPP/ZPP+RFTB groups showed a significant decrease in supine AHI (table 3). A potential reason for this difference could be the small number of patients Katsantonis et al. studied compared to our study. Lee et al. studied the effect of sleep position on surgical outcomes of UPPP in 69 consecutive patients.[40] After categorizing the patients into four groups according to the change in AHI after surgery, they found that the failure group had a higher proportion of supine position dependency. We categorized the patients in 2 groups (success[35]/failure (defined as all other patients)) but could not find significant differences in position dependency between groups. We found statistical significant differences in AHI, supine AHI and non-supine AHI for the successful group, whereas no significant differences were found in AHI, supine AHI and non-supine AHI for the failure group (data not shown here). We did not further divide our failure group into a response, non-response or true failure group like Lee et al. did so this might explain our different results. In a second paper published by the same group, results show that UPPP is a successful treatment for obstructive events occurring in the lateral sleep position, especially in patients without positional dependency.[39] Our results are in line with their finding that palatal surgery results seem better

in NPOSAS patients (success rate[35] for POSAS patients was 35.3%, for NPOSAS patients 43.7%). There are some limitations of our study which need to be addressed. Our study population included patients who concomitantly underwent RFTB. Ideally we would have studied isolated UPPP or ZPP patients. However, most patients suffered from multilevel obstruction (58.3%) and when we compared outcome of isolated palatal surgery to palatal surgery in combination with RFTB we found the percentage of supine sleeping time to be the only significant difference between groups (table 3). In addition, overall treatment was successful as defined by Sher in 39.6% of patients and only 19.4% of patients were 'cured' (AHI <5). However, our data inclusion was biased since many patients with mild OSAS who did clinically well after surgery, had no repeat PSG at all. This was due to national guidelines which state that in a patient with an initial AHI< 15 and clinical improvement, repeat PSG is not mandatory. Furthermore, reviewing all patients in whom UPPP was performed, we noticed a substantial number of patients with an AHI>15 who were not motivated for repeat PSG because of their convincing subjective improvement. The here reported overall clinical outcome might be too low because of this bias. However, evaluating effectiveness of palatal surgery was not the purpose of this study. Using a hypothesized ideal PT flowchart in which ideal positional therapy (PT) was applied in POSAS patients the success rate for our 139 patients increased to 71.2% and cure rate to 53.2%. There are some limitations of our hypothesized ideal PT flowchart. We assumed AHI values did not change after PT. This could be true but night-to-night variability is a known problem in diagnosing OSAS. Also, we assumed an ideal PT compliance of 100%. Long-term compliance with the tennis ball technique was shown to be less than 10%.[41] For the recently introduced forms of positional therapy[30,32] long-term compliance remains to be investigated.

Furthermore, our theoretical ideal PT was able to fully eliminate the supine sleep time whilst not affecting other body specific AHI values. In 2 recent studies by our group we showed the median percentage of supine sleep time to decrease from 37.9 to 6.5%[32] and from 49.9 to 0.0%[30] in 2 groups of 30 POSAS patients. Eliminating supine sleep time to 0% seems within reach. Sleep disordered breathing has been proven to be associated with increased mortality and high cardiovascular risk and therefore needs treatment.[42] In patients who cannot use or simply refuse first-line therapy (CPAP) alternative treatment is indicated. Although surgical therapy does not always cure OSAS, it has shown to provide significant benefits. OSAS surgery improves disease severity, reduces mortality and cardiovascular risk.[43,44] However, complications following OSAS surgery are not uncommon. Furthermore, efficacy of surgical treatment in terms of AHI decrease leaves room for improvement. Our present study shows palatal surgery to yield better results in terms of AHI decrease in NPOSAS than in POSAS patients. In line with the good results of our theoretical ideal PT model we therefore would suggest to use PT as a first line treatment in POSAS patients and especially the mild POSAS patients without comorbid conditions (e.g. coronary artery disease, cerebrovascular accident). Only after failing this trial with PT, either based upon symptoms or follow-up PSG with therapy in place should surgery be considered.

The variable compliance, success and cure rates seen up to now in OSAS treatment in general would not be found acceptable in other prevalent diseases such as hypertension, coronary artery disease, or diabetes. Use of both monotherapy and combined therapies has become standard in

the treatment of these other diseases.[45] OSAS patients might benefit from these complementary and collaborative treatment regimens as well.[46]

Fifty-six percent of patients with OSAS are positional; POSAS more often occurs in mild to moderate than in severe OSAS and an additional 30% suffers from evident aggravation of their AHI in supine position. Based upon the findings presented in this present study we would like to suggest using PT as first treatment in POSAS patients (without comorbid conditions as coronary artery disease and cerebrovascular accident) and only after failing this considering them for surgery. The effects of PT combined with surgery need more study.

CONCLUSION

UPPP or ZPP with or without concomitant RFTB significantly reduces overall and body position specific AHI values and should be considered in patients who do not tolerate or want CPAP or oral device therapy. In NPOSAS patients AHI reduction seems more pronounced when compared to POSAS patients. This finding further strengthens the need to consider and when possible apply positional therapy in POSAS patients. The hypothesized treatment flowchart described in this article in which positional therapy is applied in POSAS patients, either as monotherapy or in addition to surgery, seems to improve treatment results dramatically. Future research, preferably prospective and controlled, should focus on the possibility of combining sleep surgery and positional therapy.

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SUMMARY, CONCLUSIONS AND FUTURE DIRECTIONS

SUMMARY

This thesis aimed to discuss the following research questions:

1. Is position recording using a trunk position sensor in overnight sleep studies sufficient?
2. What are the short-term effects of novel positional therapies consisting of devices capable of producing a vibrational stimulus upon detection of the supine sleep position?
3. How is the long-term compliance and effectiveness of this novel positional therapy?
4. Can positional therapy increase treatment efficacy in patients in whom OSAS surgery is considered or already performed?

To be able to distinguish POSAS from non-POSAS patients, accurate sleep position measurement is of utmost importance. **Chapter 1** describes a group of 300 patients referred for polysomnography because of clinically suspected OSAS. In these patients sleep position was measured using both the standard trunk position sensor attached to the sternum as well as an extra position sensor placed on the middle of the forehead just above the eyebrows. It was found that head position, separately from trunk position, is an additional important factor in the occurrence of apneas and hypopneas in a subpopulation of OSAS patients. 41% of the studied OSAS patient group suffered from non-positional OSAS, 6.5% of OSAS patients suffered from a strictly isolated head position-dependent POSAS and 52% was position-dependent as defined by trunk position monitoring (classical POSAS). 46% of these classical POSAS patients suffered from a head supine position-aggravated POSAS, defined as an apnea hypopnea index (AHI) in head supine position which exceeded the AHI in trunk supine position by ≥5/h. These findings indicate that when studying sleep-related breathing events trunk and head position are not the same in a significant proportion of patients and that trunk position-based data may underestimate the effects of position on respiratory events.

An extensive systematical review of the literature on POSAS and positional therapy (PT) is given in **chapter 2**. It shows that sixteen studies reported on effects of PT in POSAS patients. All studies reported a positive and significant effect of PT on AHI in short-term. However, long-term compliance was found to be low. This was mainly caused by ineffectiveness, backache, discomfort and no improvement in sleep quality or daytime alertness. Consequently, there is a need for both technical improvements of PT devices as well as for further research.

Chapter 3 describes a novel yet simple neck-worn device aiming to influence sleep position and thereby treating sleep apnea in POSAS patients. The device consisted of a position sensor, *on/off* switch, small batteries and a silent alarm that would vibrate when supine position was detected. The device would vibrate with gradually incremental strength for as long as it took to detect another sleep position. In a group of 30 consecutively recruited mild to severe POSAS patients effects of wearing the device randomly switched *on* and *off* were evaluated. 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 mean AHI improved from 27.7 (no device) to 12.8/h (*on*), percentage of total sleep time in supine position from 40.0 to 19.0% (the median percentages of

total sleep time in supine position were 37.9% (no device) and 5% (*on*)), arousal index from 9.0 to 6.8/h and the number of awakenings changed from 3.4 to 4.1, but this change was non-significant.

In line with the technology of using a vibrating device to correct patients from sleeping in the supine position and its encouraging results (chapter 3) a new medical device appropriate for wide clinical use and aiming to be a more comfortable PT option was developed; the Sleep Position Trainer (SPT). The SPT is a small, lightweight (25g) device which is worn around the chest in a neoprene strap. The device measures orientation using a three-dimensional digital accelerometer. The device responds to detection of the supine position with a vibrational stimulus that continues until non-supine position is detected. If the patient does not react to the stimulus the vibrations will be paused and reinitiated after two minutes. The SPT has an internal memory to store the sleep positions of the user for a period of at least 90 days. The device employs a USB port to communicate data to a personal computer and to recharge the integrated battery. Effects, both subjective and objective, of using the SPT for one month in a group of 31 previously untreated mild to moderate POSAS patients are reported in **chapter 4**. Median percentage of supine sleep time decreased from 49.9 to 0.0%. Median AHI decreased from 16.4 to 5.2/h. 15 Patients developed an overall AHI<5. Epworth sleepiness scale (ESS) decreased from 11 to 9, functional outcomes of sleep questionnaire (FOSQ) increased from 86.0 to 93.8. The compliance was 100% with an average use of 6.4 hours per night.

Chapter 5 describes long-term effectiveness, compliance and effects on subjective sleep in a group of 106 mild to moderate and previously untreated POSAS patients. Patients were recruited from 18 Dutch hospitals and followed up for 6 months after start of SPT use. Median percentage of supine sleep time decreased from 21 to 3%. Median SPT use during 6 months was 5.5 hour per night. SPT compliance, in line with CPAP's compliance definition of more than 4 hours of nightly use, was 64.4%. Regular use, defined as more than 4 hours of usage over 5 nights/week was 71.2%. Median ESS decreased from 11 to 8, Pittsburgh sleep quality index decreased from 8 to 6 and FOSQ improved from 87 to 103.

In moderate to severe OSAS patients CPAP is regarded as the gold standard treatment with mandibular repositioning appliance (MRA) or surgery in reserve for CPAP failures. However, a substantial proportion of patients do not tolerate CPAP and/or MRA. A variety of site-specific surgical techniques has been developed. Success rates for isolated palatal and tongue base surgery vary and range from 30 to 60%. Chapters 6 and 7 aim to elucidate the role of sleep position as a confounding factor for surgical success. Furthermore, effects of surgery on body position specific AHI values as well as efficacy of treatment in both POSAS and non-POSAS patients are evaluated. 130 Moderate to severe OSAS patients who had undergone tongue base surgery (consisting of at least a hyoidthyroidpexia (HTP) procedure) were reviewed in **chapter 6**. 65 Patients had a successful reduction in either AHI or apnea index (AI). Tongue base surgery was as successful on the supine AHI as it was on the non-supine AHI. Surgery was, albeit not significantly, less successful in the POSAS patients (35.7%) compared to the non-POSAS patients (40.0%) in terms of AHI reduction. Successful and non-successful surgical results could not be explained by variations in percentages of supine sleep position. The results of tongue base surgery leave room for improvement, possibly by means of PT.

139 Mild to severe OSAS patients who had undergone palatal surgery (consisting of at least uvulopalatopharyngoplasty (UPPP) or Z-palatoplasty (ZPP)) were reviewed in **chapter 7**. Median AHI decreased from 18.0 to 11.2. Median AHI in all separate positions decreased as well. In 71 non-POSAS patients the AHI decrease was more pronounced (median AHI from 23.0 to 11.0 per hour sleep) when compared to the 68 POSAS patients (median AHI from 15.5 to 11.5 per hour sleep). This finding further strengthens the need to consider and when possible apply PT in POSAS patients. Finally, a theoretical model using an ideal form of PT was applied to patients' polysomnographical data to evaluate the possible beneficial effects of this combination or alternation of surgery and PT on outcome in terms of AHI. Using this treatment regimen the overall median AHI decreased from 18.0 to 4.5, with 53.2% of patients being 'cured' from their OSAS based on AHI<5.

CONCLUSIONS AND FUTURE PERSPECTIVES

All chapters presented in this thesis illustrate the importance of position measurement in sleep studies. The data presented in chapter 1 suggest that sleep studies should routinely include monitoring of head position, in addition to body position, since head rotation was found to be an important mediator of the severity of OSAS in terms of AHI.[1] Neck flexion and extension may be equally as important in mediating the AHI since their effects on pharyngeal collapsibility have been studied. [2-4] These head position data may be particularly important in patients undergoing a repeat sleep study following an OSAS intervention. In these patients the percentage of time sleeping in various head and body positions needs to be reported in order to determine if the intervention has been effective. Changes in head position may explain why the AHI is higher during certain portions of the night even though the body position and sleep stage are unchanged. Night-to-night variability in AHI[5,6] is likely related to changes in head position. While these findings will likely change the way overnight sleep studies are routinely performed in the future,[7] so far and to our best knowledge none of the currently available polysomnography or polygraphy devices is equipped with double position sensors. This methodological advance should be implemented not only for our in-hospital sleep studies, but also for home sleep studies.

Most, if not all, overnight in-hospital sleep studies will monitor body position. However, the majority of home sleep studies or portable monitors is not able to detect even body position.[8] With the global increase of obesity, the growing awareness for OSAS and its associated risks and the likely increase of home sleep studies in the diagnostic work-up of patients suspected of suffering from OSAS in the future,[9] recommendations by the national and international sleep societies regarding the use of portable monitors should emphasize or even better request the use of at least body position sensors. This could lead to a system of approved and validated portable monitors, more uniformity in systems used, interchangeability of results between sleep specialists and better diagnostic capabilities.

To be able to distinguish a positional from a non-positional OSAS patient is an important feature since it can help predict site of upper airway obstruction, possible treatment choices and outcome of therapy. Our group has previously shown in a group of 100 consecutive patients who underwent

drug-induced sleep endoscopy (DISE) that tongue base obstruction or epiglottis obstruction, albeit not statistically significant (P=0.058), is associated with POSAS.[10] Since the majority of POSAS patients suffers from a mild OSAS (AHI 5-15/h) the choice of treatment consists of positional therapy, MRA and surgery. MRAs have been shown to be more effective in patients with positional OSAS than in patients without positional OSAS.[11-14] Palatal surgery (UPPP) seems to enhance the positional effect on OSAS and seems to be less effective in POSAS compared to non-POSAS patients.[15-18] Tongue base surgery seems to be more effective in non-POSAS compared to POSAS patients although this finding[19] needs to be further investigated. In moderate to severe POSAS patients CPAP can be the treatment of choice. In POSAS patients auto adjusting CPAP (APAP) is preferred over fixed pressure CPAP since the positive airway pressure needed in the supine position is greater than that needed in the non-supine positions. Patients complaining of leaking masks or too high airway pressures are likely to become non-compliant to their treatment.

The detrimental effect of sleeping in supine position on the severity and frequency of apnea and hypopnea events during sleep is a well-known phenomenon. In two comparative studies of large groups of patients seeking treatment it was shown that patients suffering from positional obstructive sleep apnea syndrome (POSAS), defined as having at least twice the number of breathing abnormalities in the supine posture compared to the lateral ones, represent more than 55% of all patients suffering from obstructive sleep apnea syndrome (OSAS). [20,21] In patients with mild to moderate OSAS, the prevalence of patients with POSAS is even higher. Since all treatment options for OSAS have their specific downsides it would be a giant leap in OSAS treatment in general if patients could be offered a reversible, comfortable and less invasive treatment option. For many years positional therapy consisted of bulky masses or tennis balls placed in one's back (chapter 3). PT was found to be an effective treatment for POSAS patients in terms of AHI decrease; however long-term compliance with these types of PT were shown to be low. In this thesis the results of PT with 2 newly developed types of PT are shown (chapters 3, 4 and 5). The treatment concept of the Sleep Position Trainer (SPT), which consists of a small apparatus that is able to register body position as well as provide active feedback effectively to its user during both night and day, seems to be the best currently available option for treating POSAS patients with PT. Whether usage of the SPT results in a learning effect and natural avoidance of the supine sleep position[22] remains to be investigated.

It's likely that in the near future more types of PT based on the treatment concepts described in this thesis will be developed. If these devices should be worn on the trunk or in the head and neck region remains to be further investigated. One can imagine that in patients suffering from a strictly head position-dependent POSAS the position sensor of the PT device should be placed in the head/neck region. If future PT devices are able to promote only rotation of the head instead of completely turning to the side with the whole body, these patients are likely to suffer less from treatment-related arousals and may experience an even higher sleep quality than with the currently available PT options.

The use of PT in treating OSAS patients is not limited to the >50%[20,21] of OSAS patients suffering from POSAS. Aging in combination with weight gain has been shown to convert POSAS patients to non-POSAS patients. Non-POSAS patients who had lost weight have

been shown to convert to POSAS patients.[23] In a proportion of non-POSAS patients it's likely that PT can become the treatment of choice after weight reduction. Since central sleep apnea syndrome patients and patients suffering from Cheyne-Stokes respiration quite often experience position-dependent occurrence of apnea and hypopnea events it is likely that these patients will benefit from PT.[24-27] Future research should investigate this further. The use of PT is not confined to a single treatment solution for the POSAS patient but can be combined with other OSAS treatment options to treat more severe POSAS and non-POSAS patients. To improve compliance in APAP or CPAP therapy PT might play a role. If severe OSAS or POSAS patients are able to avoid sleeping in supine position patients would likely need lower positive airway pressures, thereby possibly improving their compliance. This assumption needs to be further investigated. The theoretical advantages of combining surgery with PT (chapters 6 and 7) need to be further elucidated in clinical trials.

Recently it was shown that in patients suffering from a mild or moderate OSAS in whom an MRA was prescribed and who suffered from a residual POSAS whilst on MRA treatment the combination of MRA with SPT showed to be more effective in terms of AHI reduction when compared to any of the single treatment options (MRA/SPT).[28] The recently introduced small embedded temperature sensing data loggers to monitor MRA compliance enhance clinical practice and research.[29] In line with the implantation of this technology into an MRA one can only wonder how long it will take before positional sensors and/or vibrational stimuli are incorporated in these devices as well.

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APPENDICES

SAMENVATTING

In dit proefschrift worden de volgende onderzoeksvragen behandeld:

1. Is positiemeting met behulp van een positiesensor op de romp voldoende bij de uitvoering van nachtelijke slaapregistraties?

2. Wat zijn de korte termijn effecten van nieuwe vormen van positietherapie (PT) die in staat zijn een vibratie te produceren op het moment dat iemand op zijn of haar rug slaapt?

3. Hoe is de lange termijn therapietrouw bij deze nieuwe vorm van PT?

4. Is het mogelijk om, bij patiënten die obstructief slaap apneu syndroom (OSAS) chirurgie aangeboden krijgen dan wel al ondergaan hebben, door middel van PT de effectiviteit van de behandeling te vergroten?

Positie-afhankelijk OSAS (POSAS) komt veel voor; meer dan de helft van de OSAS patiënten lijdt aan POSAS. POSAS kan gedefinieerd worden als OSAS in combinatie met minimaal tweemaal zoveel nachtelijke ademstops (apneus) dan wel episodes met oppervlakkige ademhaling (hypopneus) in rugligging vergeleken met de andere slaaphoudingen. Om positie-afhankelijke OSAS (POSAS) van niet-positie-afhankelijke OSAS (non-POSAS) patiënten te kunnen onderscheiden dient bepaling van de slaaphouding zeer accuraat plaats te vinden. **Hoofdstuk 1** beschrijft een groep van 300 patiënten die voor een nachtelijke slaapregistratie (polysomnografie, PSG) verwezen werd in verband met het klinische vermoeden dat OSAS de veroorzaker was van hun klachten. Bij deze patiënten werd de slaaphouding zowel met de standaard positiemeting op de romp als met een extra positiemeter op het midden van het voorhoofd, juist boven de wenkbrauwen, bepaald. Hoofdpositie, los van romppositie, bleek een belangrijke factor in het vóórkomen van apneus dan wel hypopneus. Bij 41% van de OSAS patiënten was sprake van non-POSAS. Bij 6.5% van de OSAS patiënten was sprake van een uitsluitend hoofdpositie-afhankelijk POSAS. 52% van de OSAS patiënten leed aan “klassiek POSAS”, POSAS gedefinieerd op basis van de romppositiemeting. Binnen deze “klassieke POSAS”-groep was bij 46% van de patiënten sprake van een POSAS dat bij hoofdpositie in rugligging duidelijk verergerde. Deze bevindingen wijzen erop dat bij de diagnostiek van nachtelijke ademhalingsstoornissen hoofd- en romppositie niet per definitie hetzelfde zijn voor wat betreft het vóórkomen van apneus en hypopneus en dat in een aanzienlijk deel van de patiënten romppositiemeting deze uitkomstmaat zal onderschatten.

In **hoofdstuk 2** wordt een systematisch literatuuroverzicht aangaande POSAS en PT gegeven. Zestien studies hebben de effecten van PT bij POSAS patiënten bestudeerd. In al deze studies werd op de korte termijn een positief en significant effect van PT op het aantal apneus en hypopneus per uur slaap (de zogenaamde apneu hypopneu index, AHI) gevonden. Lange termijn therapietrouw, echter, was laag. Dit werd voornamelijk veroorzaakt doordat het slapen met over het algemeen een grote massa op de rug om rugligging te voorkómen tot gevolg had dat patiënten de therapie oncomfortabel, ineffectief en rugpijn opwekkend vonden zonder dat een verbetering van slaapkwaliteit kon worden waargenomen. Dientengevolge is technische verbetering van PT apparaten en toekomstig onderzoek naar PT wenselijk.

In **hoofdstuk 3** wordt een simpel en nieuw type PT getoond ten behoeve van POSAS patiënten. Het apparaatje, dat in de nek gedragen werd, bestond uit een positiesensor, een *aan/uit*-knop, een drietal kleine batterijen en een trilalarm zoals gebruikt in mobiele telefoons. Het apparaat trilde nadat rugligging werd vastgesteld en totdat een andere slaaphouding was aangenomen. In een groep van 30 achtereenvolgend geïncludeerde licht tot matig ernstige POSAS patiënten werden de effecten van het, willekeurig ingedeeld, in *aan-/uit*-modus dragen van het apparaat geobjectiveerd. In 3 patiënten werkte het apparaat niet naar behoren: hoewel patiënten in rugligging lagen, trilde het apparaat niet. De gemiddelde AHI daalde van 27.7 (geen PT) naar 12.8 (PT *aan*) per uur slaap. Het percentage rugligging daalde van 40.0 (geen PT) naar 19.0% (PT *aan*) met mediane percentages rugligging van respectievelijk 37.9% en 5%). Het aantal *arousals* of ontwaakreacties per uur slaap daalde van 9.0 naar 6.8; het aantal momenten van daadwerkelijk wakker worden 's nachts veranderde van 3.4 naar 4.1 per nacht, maar dit was geen significant verschil.

In het verlengde van het hiervoor gepresenteerde apparaat dat in staat bleek met behulp van een trilling iemand te kunnen sturen om niet op de rug te slapen werd een nieuw apparaat, de *Sleep Position Trainer* (SPT), ontwikkeld. Therapietrouw van traditionele vormen van PT (bijv. de "tennisbaltechniek") was in het verleden laag mede doordat patiënten de behandeling als oncomfortabel bestempelden. De SPT werd gedacht een veel elegantere en comfortablere optie te zijn dan ons in hoofdstuk 3 beschreven apparaat.

De SPT is een klein, plat, lichtgewicht (25g) apparaat dat gedragen wordt in een elastische band rond de middel. Het apparaat meet de oriëntatie in de ruimte middels een digitale driedimensionale versnellingsmeter. Wanneer rugligging vastgesteld wordt reageert het apparaat met een vibratie die doorgaat totdat een andere slaaphouding dan rugligging vastgesteld is. Als de patiënt niet op de vibratie reageert, zullen de vibraties twee minuten later opnieuw aangeboden worden, zo nodig met een andere trillingssterkte. De SPT beschikt over een intern geheugen om het slaapgedrag van tenminste de afgelopen 3 maanden te bewaren. Verder kan het apparaat middels een USB-verbinding op de computer worden aangesloten om de data uit te lezen en de batterij op te laden. **Hoofdstuk 4** beschrijft de subjectieve en objectieve resultaten van het slapen met de SPT gedurende 1 maand in een groep van 31 eerder onbehandelde licht tot matig ernstige POSAS patiënten. Het mediane percentage rugligging daalde van 49.9 naar 0.0%. De mediane AHI daalde van 16.4 naar 5.2 per uur slaap. Vijftien patiënten hadden een AHI van minder dan 5 ontwikkeld en voldeden daarmee niet meer aan de definitie van OSAS. Maten van subjectieve slaperigheid, de *Epworth sleepiness scale* (ESS) en de *functional outcomes of sleep questionnaire* (FOSQ) veranderden van 11 naar 9, respectievelijk van 86.0 naar 93.8, duidend op de positieve veranderingen zoals beleefd door de patiënten. Het gemiddeld gebruik was 6.4 uur per nacht en de therapietrouw, gedefinieerd als méér dan 4 uur nachtelijk gebruik voor alle nachten, was 100%.

In **hoofdstuk 5** worden de lange termijn therapietrouw, effecten op percentage rugligging en effecten op subjectieve slaapbeleving beschreven in een groep van 106 licht tot matig ernstige eerder onbehandelde POSAS patiënten. Patiënten werden vanuit 18 Nederlandse ziekenhuizen geïncludeerd en vervolgd gedurende zes maanden na start van SPT-behandeling. Mediane percentage rugligging daalde van 21 naar 3%. Mediaan SPT-gebruik gedurende de zes maanden was 5.5 uur per nacht. De lange termijn therapietrouw was 64.4%. Regelmatig gebruik,

gedefinieerd als méér dan 4 uur gebruik gedurende 5 nachten per week, was 71.2%. Mediane ESS daalde van 11 naar 8, FOSQ steeg van 87 naar 103 en een andere subjectieve slaapgerelateerde vragenlijst, de *Pittsburg sleep quality index* daalde van 8 naar 6. De uitslagen van deze subjectieve slaapgerelateerde vragenlijsten tonen dat lange termijn SPT-gebruik is geassocieerd met een verminderde vermoeidheid overdag en een hogere slaapgerelateerde kwaliteit van leven.

Voor patiënten met een matig ernstig tot een ernstig OSAS geldt continue positieve luchtwegdruk beademing (CPAP) als gouden standaard behandeling. Mandibulaire repositie apparaten (MRA) en chirurgie kunnen bij deze patiënten bewaard worden voor die patiënten die CPAP niet kunnen verdragen. Er zijn verschillende operatieve technieken, rekening houdend met de plaats van obstructie in de bovenste luchtweg, om patiënten met OSAS chirurgisch te helpen. Echter, succespercentages van geïsoleerde ingrepen aan zachte verhemelte dan wel tongbasis variëren en liggen ergens tussen de 30 en 60%. Effecten van chirurgie op slaaphouding specifieke AHI-waarden en effectiviteit voor POSAS en non-POSAS patiënten worden geëvalueerd in hoofdstukken 6 en 7. Dit om te verhelderen of slaaphouding een vertekenende factor van chirurgisch succes is. Honderddertig matig ernstige en ernstige OSAS patiënten die tongbasis chirurgie (tenminste bestaand uit een zgn. hyoïdthyroïdpexie) hadden ondergaan worden beschreven in **hoofdstuk 6**. Vijfenzestig patiënten hadden een succesvolle afname in ofwel de AHI ofwel de apneu index. Tongbasis chirurgie had net zoveel effect op de AHI in rugligging als op de AHI in de andere slaaphoudingen. Chirurgie, alhoewel niet statistisch significant, was minder succesvol qua afname in AHI bij de patiënten die preoperatief POSAS hadden. Succesvolle en niet-succesvolle chirurgische resultaten konden niet verklaard worden op basis van variaties in percentage rugligging. De resultaten van tongbasis chirurgie zijn vatbaar voor verbetering, mogelijk door middel van PT.

Honderdnegenendertig lichte tot ernstige OSAS patiënten die een operatie aan het zachte verhemelte hadden ondergaan (tenminste een uvulopalatopharyngoplastiek of een Z-palatoplastiek) worden beschreven in **hoofdstuk 7**. De mediane AHI daalde van 18.0 naar 11.2 per uur slaap. Ook de mediane AHI in alle verschillende slaaphoudingen daalde. Bij de 71 non-POSAS patiënten was de AHI-daling uitgesprokener (mediane AHI van 23.0 naar 11.0 per uur slaap) dan bij de POSAS patiënten (mediane AHI van 15.5 naar 11.5 per uur slaap). Deze bevinding benadrukt nog eens verder het in overweging moeten nemen van PT als behandelingsoptie voor POSAS patiënten. Tot slot werd een theoretisch model, waarin gebruik gemaaktwerd van “de ideale PT”, toegepast op de polysomnografie data van de patiënten. Dit om te bezien of uitsluitend PT dan wel de combinatie van PT en chirurgie een positief effect zou hebben op de AHI daling. Als op deze manier PT vaker ingezet zou zijn bij deze groep patiënten zou de AHI gedaald zijn van 18.0 naar 4.5 per uur slaap, waarbij 53.2% van de patiënten dan een AHI kleiner dan 5 per uur slaap zou hebben en dus niet meer zou voldoen aan de diagnose OSAS.

LIJST MET AFKORTINGEN

AASM	American Academy of Sleep Medicine
AHI	apnea hypopnea index
AI	apnea index
APAP	auto adjusting continuous positive airway pressure
BMI	body mass index
BS	bariatric surgery
CPAP	continuous positive airway pressure
DI	desaturation index
DISE	drug-induced sleep endoscopy
DOFF	device *OFF*
DON	device *ON*
ESS	Epworth sleepiness scale
FOSQ	functional outcomes of sleep questionnaire
HTP	hyoidthyroidpexia
IQR	interquartile range
MMA	maxillomandibular advancement
MRA	mandibular repositioning appliance
ND	no device
NPOSAS	non-positional obstructive sleep apnea syndrome
OSA(S)	obstructive sleep apnea (syndrome)
POSAS	positional obstructive sleep apnea syndrome
PG	polygraphy
PSG	polysomnography
PT	positional therapy
RDI	respiratory disturbance index
REM	rapid eye movement
RERA	respiratory effort-related arousal
RFTB	radiofrequent ablation of the base of tongue
SD	standard deviation
SPT	Sleep Position Trainer
TBT	tennis ball technique
TST	total sleep time
UPPP	uvulopalatopharyngoplasty
ZPP	Z-palatoplasty

DOCTORAAT PORTFOLIO

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Voordrachten voortgekomen uit doctoraat

Mondeling

2009	Hyoid suspension with and without radiofrequency of the tongue base. *Surgery, Sleep and Breathing III, an International symposium, Amsterdam.*
2010	Nieuwe behandeling positiegebonden OSAS. *KNO vergadering, Nieuwegein.*
2011	Kwantitatieve effecten van borst- en hoofdpositie op de apneu hypopneu index bij obstructieve slaapapneu. *KNO vergadering, Groningen*.
2012	Positietherapie voor positiegebonden OSAS. *Verwijzersavond Mond- en Kaakziekten, AMC, Amsterdam.*
2012	- Quantitative effects of trunk and head position on the apnea hypopnea index in obstructive sleep apnea. - New simple treatment for positional OSA. *Sleep, Surgery & Breathing V, an International Symposium, Venetië.*
2012	- Quantitative effects of trunk and head position on the apnea hypopnea index in obstructive sleep apnea. - The Sleep Position Trainer: a new treatment for positional obstructive sleep apnoea. *Annual Meeting of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery, Mainz.*
2012	- Quantitative effects of trunk and head position on the apnea hypopnea index in obstructive sleep apnea. - A new simple treatment for positional OSA. - The Sleep Position Trainer: a new treatment for positional obstructive sleep apnoea. *X World Congress on Sleep Apnea, Sleep Respiratory Disorders and Snoring, Rome.*
2012	Slaap Positie Trainer: nieuwe behandeling positie-afhankelijk OSAS. *KNO vergadering, Nieuwegein.*
2013	- Diagnosis and treatment of OSA in the Netherlands. *Fudan University ENT meeting, Fudan Eye and ENT hospital, Shanghai.*

2013 Role of ENT surgeon in OSAS: diagnosis, treatment and future directions.
Philips Research Asia, Shanghai.

2013 Lange termijn evaluatie van positietherapie met de Sleep Position Trainer voor de behandeling van positieafhankelijk obstructieve slaap apneu syndroom.
KNO-vergadering, Maastricht.

2013 Positietherapie.
OSAS mini-cursus, Amsterdam.

2014 Nieuwe chirurgische behandelingen OSAS.
Refereeravond kaakchirurgie, Slotervaartziekenhuis Amsterdam.

2014 Positietherapie.
Werkgroep Ademhalingsstoornissen tijdens de Slaap, Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose, Utrecht.

2014 Long-term evaluation of positional therapy with the sleep position trainer (SPT).
Österreichische Gesellschaft für Schlafmedizin und Schlafforschung, Graz.

2014 Positietherapie.
OSAS mini-cursus, Amsterdam.

2014 Positietherapie.
Sleepless 2014, Utrecht.

2014 The Sleep Position Trainer: a new treatment for positional obstructive sleep apnea.
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2014 Positietherapie.
Speerpuntencursus, Garderen.

2014 Positietherapie.
Najaarssymposium Nederlandse Vereniging voor Slaap- en Waak Onderzoek, Sint-Michielsgestel.

Poster

2008 Van Maanen JP, Ravesloot MJL, Smits F, de Vries N, van Wagensveld BA.
Bariatric Surgery and Obstructive Sleep Apnea Syndrome (OSAS).
Wetenschapsdag, Sint Lucas Andreas Ziekenhuis Amsterdam.

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Wetenschapsdag, Sint Lucas Andreas Ziekenhuis Amsterdam.

Prijzen voortgekomen uit doctoraat

2008 Posterprijs Wetenschapsdag 2008, Sint Lucas Andreas Ziekenhuis Amsterdam.

2012 KNOwHOW jaarprijs 2011, Groningen.

2014 Tweede prijs dr. Keeman Wetenschapsprijs, Sint Lucas Andreas Ziekenhuis, Amsterdam.

2014 Junior Member Grant, European Rhinologic Society and International Symposium of Infection & Allergy of the Nose, Amsterdam.

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CURRICULUM VITAE

Peter van Maanen was born in Haarlem, the Netherlands on September 14, 1980. He graduated from university preparatory education (Mendelcollege, gymnasium) in 1998. Following graduation he studied Chemistry at VU University, Amsterdam. In 1999 he was able to switch to Medicine at the same university. In 2003-2004 he spent a 10-month period in Melbourne, Australia and was involved in breast cancer vaccine research under supervision of prof. Vasso Apostolopoulos. In 2006 he obtained his M.D. degree. In 2007 he started as a research fellow at the department of otolaryngology and head and neck surgery of the St Lucas Andreas hospital in Amsterdam to work on this thesis under supervision of prof. De Vries. In September 2008 he started his otolaryngology residency at the Academic Medical Center, Amsterdam (prof. Fokkens and prof. Van der Baan) with internships in Flevo hospital, Almere (dr. Vleming), Dutch Cancer Institute Antoni van Leeuwenhoek, Amsterdam (prof. Balm), St Lucas Andreas hospital, Amsterdam (prof. De Vries) and the Fudan Eye and ENT hospital, Shanghai, China (prof. Wang). This final internship focussed on endoscopic sinus and skull base surgery. He certified as an Otolaryngologist in May 2013. In 2014 he started working at the Slotervaart hospital Amsterdam.

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Mediq Tefa, *http://www.mediqtefa.nl*
MediTop, *http://www.meditop.nl*
MLINE, *http://www.mline.nl*
Nederlandse vereniging voor Slaap- en Waak Onderzoek, *http://www.nswo.nl*
Olympus, *http://www.olympus-global.com/en/corc/company/medical*
Snurkpoli, *http://www.desnurkpoli.nl*
Specsavers, *http://www.specsavers.nl*

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