Sleep and Breathing (2019) 23:235–241
https://doi.org/10.1007/s11325-018-1689-4

SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Patient experience with upper airway stimulation in the treatment of obstructive sleep apnea

Benedikt Hofauer[1] · Armin Steffen[2] · Andreas Knopf[1] · Katrin Hasselbacher[2] · Clemens Heiser[1]

Received: 1 February 2018 / Revised: 2 June 2018 / Accepted: 19 June 2018 / Published online: 28 June 2018

Abstract

Objective Selective upper airway stimulation (sUAS) is a new treatment modality for patients with obstructive sleep apnea (OSA) and continuous positive airway pressure (CPAP) failure. The aim of this study was to analyze therapy adherence and to structure patient experience reports.

Methods Patients from two German implantation centers were included. Besides demographic and OSA characteristics of that cohort, patients answered a questionnaire on subjective sensation of the stimulation, use of different functions, side effects, and an inventory for the description of the attitude towards sUAS. The use of the sUAS was evaluated as a read-out of the implanted system.

Results The overall apnea-hypopnea-index (AHI) of that 102 assessed patients reduced from initially 32.8/h to 12.6/h at the last available assessment. The responder rate was 75%. There was an objective therapy usage of 5.7 h and subjective reports of 6.8 nights per week. The attitude resulted in strong agreement towards the statement "UAS reduces the problems caused by my sleep apnea". Information on sensing the stimulation and usage habits could be gathered such as that stimulation is only sensed by 67.9% of the patients upon waking in the morning and that 73.6% of the patients do not change the voltage in general.

Conclusion This investigation on the sUAS therapy revealed a high adherence to the therapy. The AHI or daytime sleepiness do not have obvious influence on adherence. Patients expressed a positive attitude towards sUAS. These patient reports upon stimulation experiences are of great help to consult candidates for sUAS in future.

Keywords Hypoglossal nerve stimulation · Sleep apnea · Adherence · Upper airway stimulation

Introduction

Obstructive sleep apnea is a common sleep-related breathing disorder, characterized by recurrent upper airway (UAW) narrowing and collapse during sleep, resulting in intermittent oxyhemoglobin desaturation and sympathetic activation [1]. This results in recurrent apneas and hypopneas with oxygen desaturations, which lead to sleep fragmentation and induce a decrease of slow wave sleep [2–4]. Consequently, patients suffer from excessive daytime sleepiness and an impaired quality of life [5]. With a rising prevalence of 6% in women and 13% in men in the USA, OSA represents the most common sleep-related breathing disorder [6, 7]. A growing body of evidence shows an association between OSA and cardiovascular and metabolic comorbidities such as hypertension, ischemic heart disease, stroke, congestive heart failure, and diabetes [8–12].

While continuous positive airway pressure (CPAP) treatment has been proven to be effective in the treatment of OSA and represents the current standard, the adherence to treatment is heterogeneous among patients [13–15]. After 5 years, merely 68% of patients continue to use CPAP therapy [15]. Recently, the main results of the SAVE (Sleep Apnea Cardiovascular Endpoints) study, which was designed to evaluate the effectiveness of CPAP therapy in the reduction of cardiovascular events among patients with OSA, were published [16]. One thousand three hundred fifty-nine patients with CPAP therapy, who were compared to 1358 patients who only received advice on healthful sleep habits and lifestyle changes to minimize OSA, used their CPAP an

✉ Benedikt Hofauer
b.hofauer@tum.de

[1] Otorhinolaryngology/Head and Neck Surgery, Klinikum rechts der Isar, Technical University Munich, Munich, Germany

[2] Otorhinolaryngology/Head and Neck Surgery, University of Luebeck, Luebeck, Germany

average of 3.3 h per night [16]. Within this large group, the use of CPAP therapy constitutes low adherence, which is, however, consistent with the CPAP use in clinical practice. This amount of usage had no significant effect on the prevention of recurrent serious cardiovascular events in comparison to the so-called "advice" arm [16, 17].

Unilateral respiration-synchronized selective stimulation of the hypoglossal nerve as treatment for patients with non-compliance with CPAP therapy has been developed and successfully implemented in the routine clinical management of OSA. The STAR (Stimulation Treatment for Apnea Reduction) trial proved the effectiveness of selective upper airway stimulation (sUAS) in the treatment of OSA and several further studies have demonstrated the beneficial effects of sUAS both respiratory parameters, sleep architecture and arousals [18–23].

The aim of this study was to analyze patient reported effects of the selective upper airway stimulation and to identify possible side effects of the nightly neurostimulation.

Material and methods

Patient selection

Patients with moderate to severe OSA (AHI > 15/h and < 65/h, central apnea index < 25%) and non-adherence to CPAP therapy were eligible for enrollment. CPAP non-compliance was determined in patients who attempted to use CPAP for several days but were not willing to proceed with therapy and already had several tries of CPAP. All consecutive patients from July 2014 to December 2016 who received an implantation of an sUAS system (Inspire II Upper Airway Stimulation System, Inspire Medical Systems, Maple Grove, MN, USA) at the two participating centers (Otorhinolaryngology/Head and Neck Surgery, Klinikum rechts der Isar, Technical University Munich and Otorhinolaryngology/Head and Neck Surgery, University Hospital Schleswig-Holstein, University Luebeck) were included in this trial. Screening included inpatient polysomnography, clinical examination, and a drug-induced sleep endoscopy (DISE) [24]. The Epworth Sleepiness Scale (ESS) was used for the evaluation of excessive daytime sleepiness [25]. Patients were excluded if the body mass index (BMI) exceeded 35 kg/m^2. Patients were excluded if pronounced anatomical abnormalities preventing the effective use of sUAS were identified during clinical examination (e.g., enlarged tonsils). Informed consent was obtained for each patient. The study was approved by the local ethics committee (Fakultät für Medizin, Ethikkommission, Technische Universität München, Germany) and registered as NCT02293746 on clinicaltrials.gov as a multicenter sub-investigation of the German post-market study.

Upper airway stimulation system—implantation, follow-up, and therapy titration

The sUAS system was implanted on the patient's right side under general anesthesia according to the previously published update on the surgical technique [26, 27]. The device was activated approximately 1 month after implantation for the detection of sensation and functional thresholds. Sensation threshold is defined as the level of voltage at which the patient first feels the stimulation. Functional threshold is defined as the level of voltage at which the patient's tongue motion is observed. Following 1 month of nocturnal accommodation, inpatient polysomnography was performed to individualize sUAS therapy by performing a titration night (month 2 post-implantation). At month 3 post-implantation, another inpatient polysomnography was conducted to ensure the stability of sUAS efficiency. Further follow-up visits, which included home sleep polygraphies (PG), were scheduled at month 6, 12, and from then on, every 12 months.

Data collection and questionnaire

Patient characteristics (age, sex, and pre- and post-implantation BMI) were collected. Two months post-implantation, an 18-channel inpatient polysomnography (PSG) according to the American Academy of Sleep Medicine (AASM) guidelines from 2012 was used for the titration of the sUAS [28]. Mean and minimal oxyhemoglobin saturation were recorded. Self-reported sleepiness was assessed using the ESS score with a score less than 10 being considered the threshold for normal subjective sleepiness. The outcome measurements and the classification of responders were defined in accordance with the criteria postulated by Sher et al. [29].

As there is no standardized protocol, a self-designed questionnaire both for the subjective amount of usage and utilization of the different function as well as the subjective sensation of the stimulation was established. The amount of use and the use of the different functions of the sUAS system were evaluated with the questions presented in Table 1. The subjective sensation of the stimulation was measured by the questions

Table 1 Questions for the evaluation of the use and the use of different functions of the sUAS

1. How many days per week do you use the sUAS? (*7, 6, 5, 4, 3, 2, 1, 0*)
2. How many hours per night do you use the sUAS? (*more than 8, 7–5, 4–2, less than 2*)
3. Do you use the pause function if you wake up during the night? (*yes/no*)
4. How often do you modify the stimulation intensity? (*never, once per month, once per week, several times per week, every day*)
5. If yes: What are the reasons for the modification? (*free text*)

Table 2 Questions for the evaluation of the subjective sensation of the stimulation

1. Can you feel the stimulation when activating the therapy? (*yes/no*)
2. Can you feel the stimulation during the night? (*yes/no*)
3. If yes: Do you wake up due to the stimulation? (*yes/no*)
4. Can you feel the stimulation when you wake up at night? (*yes/no*)
5. If yes: How do you experience the stimulation? (*disruptive, non-disruptive, variable*)
6. How often do you turn off the stimulation during the night and continue to sleep without sUAS? (*never, once per week, more than once per week, every day*)
7. If yes: What are the reasons for turning off the therapy? (*free text*)
8. Do you feel the stimulation in the morning? (*yes/no*)
9. How often do you forget to turn off the therapy in the morning? (*never, once per week, more than once per week, every day*)

presented in Table 2. Side effects of the sUAS were recorded with the questions included in Table 3. The attitude to sUAS was measured by adopting the attitudes to CPAP treatment inventory (ACTI) containing the questions presented in Table 4 [30].

Statistical analysis

Version 24.0 of the Statistical Package for the Social Sciences software (SPSS, Chicago, IL, USA) was used. Descriptive statistics were calculated for demographic variables. Paired *t* test was used to compare baseline and post-implantation values. Data are given as mean ± standard deviation. Spearman's rank correlation coefficient (*r*) was used for the analysis of correlations (0.80–1.00 = very strong correlation, 0.60–0.79 = strong correlation, 0.40–0.59 = moderate correlation, 0.20–0.39 = weak correlation, and 0.00–0.19 = very weak correlation). *P* values of ≤ 0.05 were considered statistically significant.

Results

Patients' characteristics and clinical outcome

The study population consisted of 102 participants who received an sUAS device at one of the two participating centers

Table 3 Questions for the evaluation of side effects of sUAS

1. Do you have any impairment after turning off the therapy in the morning? (*never, once per week, several times per week, every day*)
2. If yes: What kind of impairment do you have? (*free text*)
3. If yes: How long does the impairment last? (*free text*)
4. Is your movement of the neck impaired? (*yes/no*)
5. Is your movement of the chest impaired? (*yes/no*)

Table 4 Description of the attitude to sUAS treatment inventory adopted from the ACTI (1 = strongly agree, 2 = agree, 3 = undecided, 4 = disagree, 5 = strongly disagree) [Broström et al. [30]

1. sUAS reduces the problems caused by my sleep apnea.
2. sUAS improves my health.
3. sUAS improves my quality of life.
4. sUAS is the best treatment for my sleep apnea.
5. I can use the sUAS as expected for me.

(Munich n=57, Lübeck n=45). The mean age was 56.7 ± 11.3 years and the mean BMI was 29.4 ± 4.3 kg/m^2. The mean BMI remained stable during the study period. The mean AHI score on pre-operative polysomnography was 32.8/h (± 13.9) and decreased at the last follow-up to 12.6/h (± 13.4; $p < 0.001$). The mean ODI decreased from a baseline value of 27.6/h (± 17.6) to 12.0/h (± 14.0; $p < 0.001$) at the last follow-up. The subjective sleepiness decreased from an ESS of 12.9 (± 4.6) at baseline to 7.0 (± 4.6) at the last follow-up. On average, patients were implanted 10.1 months before the investigation on adherence of OSA was conducted. Table 5 provides an overview on the number of patients at the different time points during the follow-up after the implantation. According to Sher criteria, 75% were responders to the sUAS regarding the reduction of the baseline AHI at the time of follow-up.

Objective and self-reported adherence to sUAS

Patients used sUAS on average 40.0 h per week (± 14.2) which results in a daily adherence of 5.7 h (± 2.0) since the sUAS device was activated 1 month after the implantation. The duration of daily activation correlated moderately both with the declared weekly and nightly use ($r = 0.433$ and $r = 0.485$ respectively, with p values of 0.024 and < 0.001), with patients stating that they activated the system an average of 6.8 days (± 0.9) per week and usually used it for 5 to 7 h per night. In patients, who declared to activate the therapy on 0–4 days per week, an objective usage of 3.9 h (± 2.7) was observed compared to patient, who declared to activate the therapy on 5–7 days per week, in whom an objective usage of 5.8 h (± 2.0) per night was observed ($p = 0.124$, Fig. 1). The analysis of the UAS device showed that 25.5% of the patients

Table 5 Illustration of the number of patients at the different time points in the follow-up after the implantation

Follow-up	Month 2	Month 3	Month 6	Month 12	Month 24	Month 36
Patients (*n*)	102	84	83	58	11	1

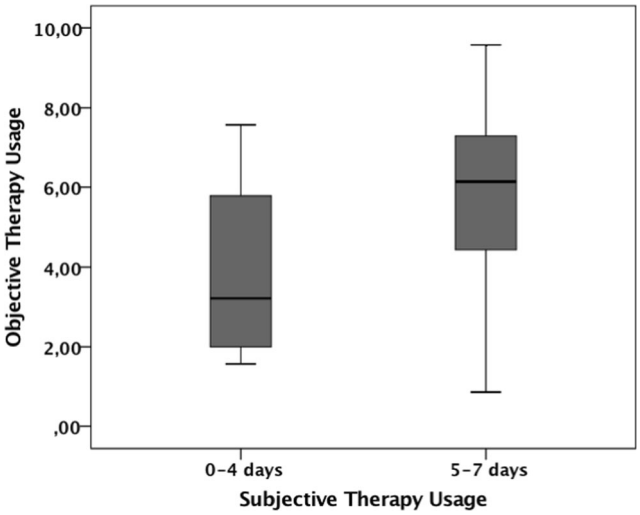

Fig. 1 The objective therapy usage per night in the group of patients subjectively using the therapy for 0–4 days per week compared to patients using the therapy for 5–7 days per week

in the reported cohort used the sUAS therapy less than 4 h per night, 74.5% for 4 h and more per night, and 50% of the patients for more than 6 h per night. The duration between the implantation and the follow-up correlated with the responder rate ($r = 0.388$, $p < 0.001$). There were significant correlations between the responder rate according to Sher and the absolute and relative reduction of the AHI ($r = 0.228$ and $r = 0.543$) and postoperative ODI ($r = -0.521$). Elder patients revealed a better adherence to the stimulation therapy ($r = 0.211$, $p = 0.42$).

The pause function is used by 59.4% of the patients during the night. In patients, who use the pause function, the nightly objective usage is less (5.4 ± 1.9 h) compared to patients, who do not use the pause function (6.2 ± 2.1 h, $p = 0.041$). The vast majority of patients (73.6%) reported never to change the intensity of the stimulation while 17.0% change the intensity once per month and 7.5% once per week. Only 2 patients change the intensity several times per week or daily. The main reasons why patients changed the stimulation intensity were infections of the upper airway, changes in the sleep environment or curiosity.

Subjective sensation and side effects of sUAS

Most patients (93/102) sense the stimulation during the activation but only 49.0% sense the stimulation during the night (50/102) with 14 out of 102 patients (13.7%) were sometimes awoken by therapy. None of the reported sensations had an influence on the objective nightly usage. When patients wake up during the night due to other reasons, 80.2% sense the stimulation. However, 22.6% of the patients found the stimulation to be disruptive. With fewer patient finding the stimulation disruptive with increasing duration between the implantation and the follow-up, a negative correlation was observed ($r = -0.200$, $p = 0.045$). Twenty out of 102 patients (19.6%) turn the therapy off during the night and continue to sleep without therapy once per week, 10 out of 102 patients (9.8%) several times per week and 2 out of 102 patients (2.0%) every night, mainly as a consequence to discomfort from the stimulation. The objective nightly usage is in patient, who turn of the therapy during the night, lower than in patients, who never turn the therapy of (4.7 ± 1.9 h versus 6.2 ± 1.9 h, $p = 0.001$). The stimulation is sensed by 67.9% of the patients upon waking in the morning with 10.8% of patients forgetting to turn therapy off in the morning (11 out of 102 patients once per week, and six of those 11 forgetting several times per week.

Twelve patients reported some kind of impairment of the tongue in the morning after a night of stimulation, with eight of the twelve reporting impairment less than once per week, three patients more than once per week and one patient daily. The most reported impairment regards movability of the tongue. Patients reported these impairments to usually persist for a few minutes. The implanted system causes an impaired movement of the neck in 4 patients (3.9%) and of the chest in 6 patients (5.9%). With fewer patient reporting impaired movement of the chest with increasing duration between the implantation and the follow-up, a negative correlation was observed ($r = -0.266$, $p = 0.007$). The information on sensation and side effects of the sUAS did not correlate with the adherence to therapy.

Attitude towards sUAS treatment

The evaluation of the attitude towards sUAS treatment resulted in a mean value of 1.44 for question 1 (coding for strong agreement towards the statement "sUAS reduces the problems caused by my sleep apnea"), a mean value of 1.52 for question 2 (coding for agreement towards the statement "sUAS improves my health"), a mean value of 1.51 for question 3 (coding for agreement towards the statement "sUAS improves my quality of life"), a mean value of 1.27 for question 4 (coding for strong agreement towards the statement "sUAS is the best treatment for my sleep apnea"), and a mean value of 1.37 for question 5 (coding for strong agreement towards the statement "I can use the sUAS as expected for me"). The results of question 1 correlated with the relative and absolute reduction of the pre-operative AHI ($r = -0.299$, $p = 0.003$ and $r = -0.244$, $p = 0.018$) and the responder rate ($r = -0.280$, $p = 0.006$). Questions 2–5 correlated weakly with the amount of nightly usage (r ranging from −0.299 to −0.238, p value ranging from 0.022 to 0.027). The results on the attitude towards the sUAS are illustrated in Fig. 2.

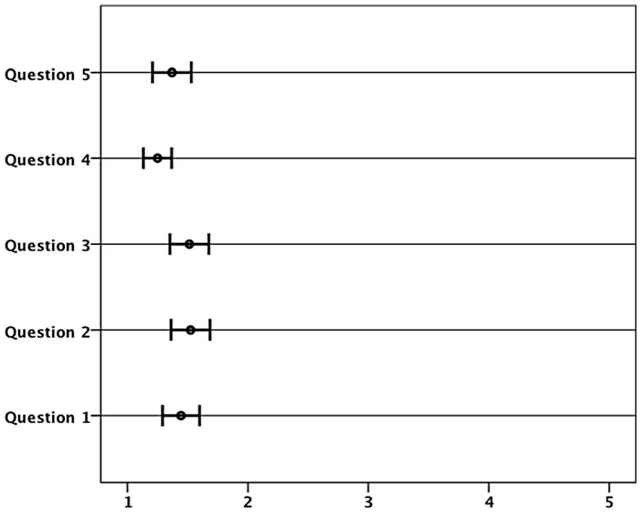

Fig. 2 Results on the attitude towards sUAS treatment adopted from the ACTI (1 = strongly agree, 2 = agree, 3 = undecided, 4 = disagree, 5 = strongly disagree) [Broström et al. [30]. The figure shows the average result and the 95% confidence interval for the particular question (mean values: question 1 = 1.44, question 2 = 1.52, question 3 = 1.51, question 4 = 1.27, question 5 = 1.37)

Discussion

Surgical procedures for the treatment of OSA usually do not require the patient's adherence, per se, since the surgical modifications of the upper airway (e.g., the velum or the tonsils) are permanent. In selective upper airway stimulation however, a voluntary adherence to the therapy is necessary to guarantee an effective treatment, since the patient needs to activate the therapy every evening—similar to CPAP therapy, whose effectiveness also depends on the patient's adherence. As sUAS represents a comparatively new treatment alternative for OSA, no detailed investigations on side effects of the neurostimulation have yet been conducted and published.

The monitoring of the objective adherence to sUAS revealed a mean usage of 5.7 h per night in our patient cohort. In some previous studies, the amount of the nightly usage has been reported. In 2014, Kezirian et al. published the 12-month results of 31 patients with an sUAS and observed that the therapy was used by the patients in 86% of the nights for 5.4 h (SD = 1.4), which is very similar to the results of our investigation [22, 31]. In 2016, Kent et al. published a single-center experience after the implantation of 20 patients and polysomnographic evaluation 2–6 months after surgery. In this cohort, the patients used the device for 7.0 h per night (SD = 2.2) [32]. In 2017, Steffen et al. published the 12-month results of the German post-market study containing 60 patients. Again, a nightly voluntary use of the device of 5.6 h, similar to the results of the findings presented above (with a partly overlap in the patients cohort), was observed [33].

In the SAVE study, the adherence to the therapy in the CPAP group was 4.4 h per night (SD = 2.2) after the first month and decreased to 3.3 h per night (SD = 2.4) after 1 year amongst the 1359 included patients. Only 42% of these patients used the CPAP therapy for more than 4 h per night during the follow-up period [16]. Similar results have previously been published, for example by Weaver et al., who observed an adherence to CPAP therapy in 17–54% of patients when using the same definition for adherence [17]. In our cohort, 74.5% of the patients activated the sUAS for more than 4 h per night and 50% of the patients for more than 6 h per night. There are no comparable rates from previously published studies on sUAS. Contrary to the observation of a decrease in nightly usage of CPAP in the SAVE study, we did not observe any decline in the adherence of patients after 2, 3, 6, 12, 24, or 36 months. A possible explanation for the superior adherence to sUAS is the intensive support which is applied to the patients, since especially during the first year several in- and outpatient visits (drug-induced sleep endoscopy, surgical procedure, post-op visits, activation of the sUAS, titration of the sUAS, and home sleep studies) are necessary and additionally, patients are offered a telephone-linked communication. These two interventions are known to promote adherence to CPAP therapy [14]. Another point might be that the access to sUAS in Germany is still restricted and only a few hospitals are certified to perform this procedure, which could increase the appreciation of the patients towards therapy. Usually, patients who apply for an implantation of an sUAS device are better educated about their disease and the associated risks of OSA—characteristics which also differentiate the adherent from the non-adherent CPAP user [14]. At our both centers, patients have a close connection to caretaking surgeons and sleep technologists, what helps to identify usage problems at an early stage or technical problems and increases chances to overcome misunderstandings. Additionally, these patients are in general probably higher motivated compared to CPAP patients in first line situation as here, patients with a higher interest to get sufficient reduction of their OSA burden came to sleep centers to evaluate whether they are candidates for sUAS or not. Those patients who have CPAP problems but as well no benefit or no subjective disease understanding would not take the demanding selection process for sUAS. Our patients are convinced of the therapy at a high amount what reflects very low scoring in the modified ACTI. This finding is nonetheless of further interest by virtue of non-compliance with CPAP being a necessary precursor to indication for this therapy, thereby skewing the population with a de facto "failure bias."

Considering the results from various studies on the effect of CPAP therapy, which could show that for normalization of sleepiness (evaluated with the ESS), improvement of quality of life and the neurocognitive function, four of more hours of use are necessary, all the reported adherence observations for sUAS in this study are well above that value [14, 34–36]. Cardiovascular disorders and diabetes have shown greater improvements in patients with a usage of more than 4 h of CPAP

per night [37–39]. Five hours of use have been shown to improve the neurobehavioral performance [35]. Six hours of use are reported to be necessary to normalize the level of objective alertness in the multiple sleep latency test [34]. For the normalization of the daytime functioning on the Functional Outcomes of Sleep Questionnaire (FOSQ), a regular use of 7.5 h per night is required [34]. There is no reason to believe that these numbers cannot be transferred to the effect of an effective sUAS therapy program. In this study and our other previously published results, the reported adherence rates were sufficient to decrease the elevated ESS values at baseline to normal limits during the therapy. Soose et al. observed a significant improvement regarding the FOSQ scale after 24 months in patients with sUAS [40].

In our cohort of 102 patients, 14 patients (13.7%) reported to wake up because of sUAS. However, in a previous published study on the effect of sUAS on sleep architecture, containing partly the same patients as in this investigation, we demonstrated that the electrical stimulation of the hypoglossal nerve did not provoke arousals but rather induced a significant overall decrease of arousals, sleep stage changes and changes during wakefulness [41]. These seeming discrepancies might be explained by an incorrect association between awake periods during the night including sensation of the stimulation, which however might not have been the cause of the awakening, rather secondary awareness upon awakening for some other reason. A possible disadvantage of our survey might be the fact that we had to established self-designed questionnaires as there is none which reflects the need intended here. As responded from the patients, many could fill in them quite easy without further explanations. Nonetheless, all the answers are done subjectively from patient's perspective. Future technology process for better data collection about voltage changes, night-to-night usage, or the number of restarts and pause function are needed for an improved insight and better therapy adherence interventions in sUAS.

In conclusion, this investigation on side effects of sUAS therapy in patients with OSA revealed a high adherence to the therapy. The usually applied thresholds, which define adherence in CPAP therapy, were achieved by 74.5% of the patients. The reported adherence rates did not differ during the observation period and neither AHI, ODI, nor ESS seemed to have an influence on adherence. Patients expressed a positive attitude towards sUAS. Information on the nightly neurostimulation could be gathered. Future studies should evaluate if high adherence to sUAS has the same effect as high adherence to CPAP therapy on cardiovascular disorders, diabetes, and neurobehavioral performance.

Acknowledgements The authors would like to express their gratitude to the study nurses and colleagues of the local sleep laboratories Sabrina Wenzel, Katharina Eckbauer, and Nicole Behn for their commitment in collecting and processing the necessary data for this study.

Compliance with ethical standards

Conflict of interest Armin Steffen and Clemens Heiser are study investigators and received honoraria, travel and research support from Inspire Medical Systems. Katrin Hasselbacher and Benedikt Hofauer received travel expenses from Inspire Medical Systems. The article submitted is related to this relationship. Andreas Knopf received research support from Optima Pharmazeutische GmbH. The article submitted is not related to this relationship.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethikkommission, Fakultät für Medizin, Technical University Munich) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participant included in the study.

References

1. Pengo MF, Steier J (2015) Emerging technology: electrical stimulation in obstructive sleep apnoea. J Thorac Dis 7:1286–1297
2. Heiser C, Knopf A, Bas M, Gahleitner C, Hofauer B (2016) Selective upper-airway stimulation for obstructive sleep apnea—a single center clinical experience. Eur Arch Otorhinolaryngol
3. Heiser C, Edenharter G, Bas M, Wirth M, Hofauer B (2017) Palatoglossus coupling in selective upper airway stimulation. Laryngoscope 127:E378–E383
4. Heiser C, Hofauer B (2017) Predictive success factors in selective upper airway stimulation. ORL J Otorhinolaryngol Relat Spec 79: 121–128
5. Strollo PJ, Rogers RM (1996) Obstructive sleep apnea. N Engl J Med 334:99–104
6. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328:1230–1235
7. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM (2013) Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 177:1006–1014
8. Narkiewicz K, Somers VK (1999) Obstructive sleep apnea as a cause of neurogenic hypertension. Curr Hypertens Rep 1:268–273
9. Martinez D, Klein C, Rahmeier L, da Silva RP, Fiori CZ, Cassol CM, Gonçalves SC, Bos AJG (2012) Sleep apnea is a stronger predictor for coronary heart disease than traditional risk factors. Sleep Breath 16:695–701
10. Lévy P, Bonsignore MR, Eckel J (2009) Sleep, sleep-disordered breathing and metabolic consequences. Eur Respir J 34:243–260
11. Punjabi NM, Sorkin JD, Katzel LI, Goldberg AP, Schwartz AR, Smith PL (2002) Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. Am J Respir Crit Care Med 165:677–682
12. Gottlieb DJ, Yenokyan G, Newman AB, O'Connor GT, Punjabi NM et al (2010) Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the sleep heart health study. Circulation 122:352–360
13. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ (2006) Continuous positive airways pressure for obstructive sleep apnoea in adults Cochrane Database Syst Rev CD001106
14. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE (2011) A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev 15:343–356

15. Stuck BA, Leitzbach S, Maurer JT (2012) Effects of continuous positive airway pressure on apnea-hypopnea index in obstructive sleep apnea based on long-term compliance. Sleep Breath 16:467–471
16. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, Mediano O, Chen R, Drager LF, Liu Z, Chen G, du B, McArdle N, Mukherjee S, Tripathi M, Billot L, Li Q, Lorenzi-Filho G, Barbe F, Redline S, Wang J, Arima H, Neal B, White DP, Grunstein RR, Zhong N, Anderson CS, SAVE Investigators and Coordinators. (2016) CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med 375:919–931
17. Weaver TE, Grunstein RR (2008) Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc 5:173–178
18. Strollo PJ, Soose RJ, Maurer JT, de Vries N, Cornelius J et al (2014) Upper-airway stimulation for obstructive sleep apnea. N Engl J Med 370:139–149
19. Strollo PJ, Gillespie MB, Soose RJ, Maurer JT, de Vries N et al (2015) Upper airway stimulation for obstructive sleep apnea: durability of the treatment effect at 18 months. Sleep 38:1593–1598
20. Heiser C, Maurer JT, Hofauer B, Sommer JU, Seitz A, Steffen A (2017) Outcomes of upper airway stimulation for obstructive sleep apnea in a multicenter German postmarket study. Otolaryngol Head Neck Surg 156:378–384
21. Van de Heyning PH, Badr MS, Baskin JZ, Cramer Bornemann MA, De Backer WA et al (2012) Implanted upper airway stimulation device for obstructive sleep apnea. Laryngoscope 122:1626–1633
22. Kezirian EJ, Goding GS, Malhotra A, O'Donoghue FJ, Zammit G et al (2014) Hypoglossal nerve stimulation improves obstructive sleep apnea: 12-month outcomes. J Sleep Res 23:77–83
23. Hofauer B, Strohl K, Knopf A, Bas M, Wirth M et al. (2016) Sonographic evaluation of tongue motions during upper airway stimulation for obstructive sleep apnea-a pilot study. Sleep breath
24. Heiser C, Fthenakis P, Hapfelmeier A, Berger S, Hofauer B, Hohenhorst W, Kochs EF, Wagner KJ, Edenharter GM (2017) Drug-induced sleep endoscopy with target-controlled infusion using propofol and monitored depth of sedation to determine treatment strategies in obstructive sleep apnea. Sleep Breath 21:737–744
25. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14:540–545
26. Heiser C, Thaler E, Boon M, Soose RJ, Woodson BT (2016) Updates of operative techniques for upper airway stimulation. Laryngoscope 126:S12–S16
27. Heiser C, Hofauer B, Lozier L, Woodson BT, Stark T (2016) Nerve monitoring guided selective hypoglossal nerve stimulation in obstructive sleep apnea. Laryngoscope 126:2852–2858
28. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, Davidson Ward SL, Tangredi MM, American Academy of Sleep Medicine. (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med 8:597–619
29. Sher AE, Schechtman KB, Piccirillo JF (1996) The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 19:156–177
30. Broström A, Ulander M, Nilsen P, Svanborg E, Arestedt KF (2011) The attitudes to CPAP treatment inventory: development and initial validation of a new tool for measuring attitudes to CPAP treatment. J Sleep Res 20:460–471
31. Hofauer B, Steffen A, Knopf A, Hasselbacher K, Heiser C (2018) Adherence to upper-airway stimulation in the treatment of obstructive sleep apnea. Chest 153:574–575
32. Kent DT, Lee JJ, Strollo PJ, Soose RJ (2016) Upper airway stimulation for OSA: early adherence and outcome results of one center. Otolaryngol Head Neck Surg 155:188–193
33. Steffen A, Sommer JU, Hofauer B, Maurer JT, Hasselbacher K, Heiser C (2017) Outcome after one year of upper airway stimulation for obstructive sleep apnea in a multicenter German post-market study. Laryngoscope
34. Weaver TE, Maislin G, Dinges DF, Bloxham T, George CF et al (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. Sleep 30:711–719
35. Zimmerman ME, Arnedt JT, Stanchina M, Millman RP, Aloia MS (2006) Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. Chest 130:1772–1778
36. Antic NA, Catcheside P, Buchan C, Hensley M, Naughton MT, Rowland S, Williamson B, Windler S, McEvoy RD (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. Sleep 34:111–119
37. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, Chiner E, Masa JF, Gonzalez M, Marín JM, Garcia-Rio F, Diaz de Atauri J, Terán J, Mayos M, de la Peña M, Monasterio C, del Campo F, Montserrat JM, Spanish Sleep And Breathing Network. (2012) Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA 307:2161–2168
38. Bratton DJ, Stradling JR, Barbé F, Kohler M (2014) Effect of CPAP on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomised controlled trials. Thorax 69:1128–1135
39. Craig SE, Kohler M, Nicoll D, Bratton DJ, Nunn A, Davies R, Stradling J (2012) Continuous positive airway pressure improves sleepiness but not calculated vascular risk in patients with minimally symptomatic obstructive sleep apnoea: the MOSAIC randomised controlled trial. Thorax 67:1090–1096
40. Soose RJ, Woodson BT, Gillespie MB, Maurer JT, de Vries N, Steward DL, Strohl KP, Baskin JZ, Padhya TA, Badr MS, Lin HS, Vanderveken OM, Mickelson S, Chasens E, Strollo PJ Jr, STAR Trial Investigators. (2016) Upper airway stimulation for obstructive sleep apnea: self-reported outcomes at 24 months. J Clin Sleep Med 12:43–48
41. Hofauer B, Philip P, Wirth M, Knopf A, Heiser C (2017) Effects of upper-airway stimulation on sleep architecture in patients with obstructive sleep apnea. Sleep Breath 21:901–908