Upper Airway Stimulation in Patients with Obstructive Sleep Apnea: Long-Term Surgical Success, Respiratory Outcomes, and Patient Experience

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Abstract

Introduction Upper airway stimulation (UAS) with electric activation of the hypoglossal nerve has emerged as a promising treatment for patients with moderate-to-severe obstructive sleep apnea.

Objective To retrospectively analyze objective and subjective outcome measures after long-term follow-up in obstructive sleep apnea patients receiving upper airway stimulation.

Methods An observational retrospective single-center cohort study including a consecutive series of patients diagnosed with obstructive sleep apnea receiving upper airway stimulation.

Results Twenty-five patients were included. The total median apnea-hypopnea index (AHI) significantly decreased from 37.4 to 8.7 events per hour at the 12-month follow-up ($p < 0.001$). The surgical success rate was 96%. Adverse events were reported by 28% of the patients.

Conclusion Upper airway stimulation is an effective and safe treatment for obstructive sleep apnea in patients with continuous positive airway pressure (CPAP) failure or intolerance. However, it is possible that the existing in and exclusion criteria for UAS therapy in the Netherlands have positively influenced our results.

Keywords
- obstructive sleep apnea
- hypoglossal nerve
- implantable neurostimulators
- electric stimulation therapy
- patient satisfaction
- treatment outcome

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Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repetitive partial or complete upper airway obstruction which often results in decreased arterial oxygen saturation and arousal from sleep.[1] The current gold standard treatment of moderate-to-severe OSA is continuous positive airway pressure (CPAP).[2] However, compliance and long-term use of CPAP is rather low.[3] Alternative treatments include custom-made oral appliance therapy (OAT), positional therapy and upper airway surgery. Since evidence-based reviews do not uniformly support the efficacy of these treatments for moderate-to-severe sleep apnea, a new therapy is desirable.[4,5] Upper airway stimulation (UAS) with electric activation of the hypoglossal nerve has emerged as a promising treatment for patients with moderate-to-severe obstructive sleep apnea who have failed CPAP. Upper airway stimulation has shown favorable success and low morbidity.[6–9] The aim of the present study was to retrospectively analyze the single-center results in terms of surgical success, respiratory outcomes, subjective outcome measures, and adverse events (AEs) in patients with OSA treated with upper airway stimulation.

Methods

Study Design and Population

An observational retrospective single-center cohort study was conducted at the department of otorhinolaryngology in the St. Antonius Hospital. Patients were included in this study if they were diagnosed with OSA and underwent implantation of an upper airway stimulation system. One-year follow-up data had to be available. In the Netherlands, the main inclusion criteria for implantation of UAS are failure of or intolerance to treatment with CPAP, an apnea-hypopnea index (AHI) between 30 and 50 events per hour, including less than 25% central apneas, and a body-mass index (BMI) $< 32\ kg/m^2$. The exclusion criteria include a complete concentric collapse at velopharyngeal level objectified during drug-induced sleep endoscopy, severe restrictive or obstructive pulmonary disease, moderate-to-severe pulmonary arterial hypertension, severe valvular heart disease, New York Heart Association class III or IV heart failure, recent myocardial infarction or severe cardiac arrhythmias (within the past 6 months), persistent uncontrolled hypertension despite medical use, active psychiatric disease, coexisting non-respiratory sleep disorders that would confound functional sleep assessment and expected future indications for a magnetic resonance imaging (MRI) scan of the chest or the abdomen.

Upper Airway Stimulation System

The UAS system (Inspire Medical Systems Inc., Maple Grove, MN) consists of a respiration sensor, programmable implanted pulse generator (IPG), and stimulating electrodes. The sensor is placed between the internal and external intercostal muscles and detects respiratory efforts from chest excursions that are analyzed by the IPG. The IPG is implanted below the clavicle and delivers stimulation synchronized with the respiratory cycle to the stimulation electrode. The stimulation electrode is placed on the anterior branches of the hypoglossal nerve and cervical spinal nerve 1 (C1). Upon stimulation, these nerves cause forward protrusion of the tongue by stimulating the genioglossus muscle. Furthermore, stimulation of C1 causes an anterosuperior displacement of the hyoid bone, both increasing the size of the oropharyngeal airway. Additionally, previous studies have shown that the effect of upper airway stimulation is not limited to the level of the tongue base, but it also improves airway patency at the level of the palate caused by palatoglossal coupling.[10,11]

Objective Outcome Measures

In-laboratory polysomnography (PSG) was performed at baseline in all patients. After implantation of the UAS in-laboratory PSG was performed at 2, 6, and 12 months. Polysomnography included electroencephalography, electrooculography, surface electromyography, nasal airflow, and air temperature, thoracoabdominal movements, pulse oximetry, body position, and snoring sounds. Breathing was recorded with nasal pressure and temperature sensors. Scoring of electronic raw data was performed manually, following the recommendations of the American Academy of Sleep Medicine.[12] Apnea was defined as a decrease of at least 90% of airflow from baseline for >10 seconds. Hypopnea was defined as a decrease of at least 30% of airflow from baseline for >10 seconds, associated with either an arousal or $\geq$ 3% arterial oxygen saturation decrease. The mean AHI was calculated. The oxygen desaturation index (ODI) $\geq$ 3% was defined as the mean number of arterial oxygen desaturations $\geq$ 3% per hour. The ODI $\geq$ 4% was defined as the mean number of arterial oxygen desaturations $\geq$ 4% per hour. Other PSG parameters collected included the apnea index (AI), the AHI in supine position, the AHI in non-supine position, and mean arterial oxygen saturation (SpO2). Patient therapy use was measured in hours per week and was collected during the in-laboratory PSG. Surgical success was defined according to the Sher criteria: a reduction in baseline AHI of more than 50%, and a postoperative AHI of less than 20 events per hour.[13] An additional classification was made for patients with a reduction in baseline AHI of more than 50% and a postoperative AHI of less than 15 events per hour. Adverse events were collected at the 6- and 12-month visits and were subdivided into procedure- and therapy-related AEs.

Subjective Outcome Measures

The Epworth sleepiness scale (ESS), which was designed to assess the extent of daytime sleepiness, was collected at baseline in all patients.[14] Additionally, all patients completed the ESS at 6- and 12-month visit. An adapted clinical global impression (CGI) scale, which was originally designed for patients with mental disorders, was used by the physician to compare the present clinical condition to baseline. The CGI ranges from 1 (very much improved) to 6 (very much worse). Furthermore, all patients received a questionnaire regarding

Table 1 Baseline characteristics

Measurement	N = 25
Male patients	24 (96%)
Age (mean ± SD; years)	62.40 ± 9.45
BMI (mean ± SD; kg/m^2)	28.18 ± 2.34
AHI (median (Q1-Q3); e/h)	37.40 (33.7–45.6)
ODI ≥4% (median (Q1-Q3); e/h)	20.10 (16.5–27.2)
ESS (mean ± SD)	10.28 ± 5.26

Abbreviations: AHI, apnea-hypopnea index; BMI, body-mass index; ESS, Epworth sleepiness scale; ODI, oxygen desaturation index; Q1, quartile 1; Q3, quartile 3; SD, standard deviation.

patient experience with therapy (PET). This questionnaire consists of four questions regarding patient satisfaction:

- How does UAS therapy compare against your previous experience with CPAP?
- What is the likelihood of choosing UAS therapy again?
- What is the likelihood of recommending UAS therapy to friends/family?
- Overall, how satisfied are you with UAS therapy?

Ethical Considerations

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Data on study subjects were collected and stored anonymously to protect personal information. Informed consent was obtained prior to data collection.

Statistical Analysis

The statistical analysis was performed by using the IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous data are presented as means with standard deviations. Non-normally distributed continuous data are presented as median with interquartile range (IQR). Categorical variables are presented as frequencies with percentages. Comparisons between groups were performed using Chi-squared tests for categorical variables, paired *t* test and Wilcoxon rank sum test for continuous variables. A two-tailed p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

This retrospective analysis consists of 25 patients undergoing implantation of upper airway stimulation between January 2018 and September 2019, baseline characteristics are mentioned in ►**Table 1**. Ninety-six percent of the patients were male with a mean age of 62.40 ± 9.45 years. The mean body-mass index (BMI) was 28.18 ± 2.34 kg/m^2. The median

Table 2 Outcome measures at 6- and 12-month follow-up

Measurement	Preoperative	Time point	Postoperative	*P*-value
AHI (median (Q1-Q3); e/h)	37.40 (33.7–45.6)	6 months	8.10 (3.9–15.0)	< 0.001*
		12 months	8.70 (4.8–12.7)	< 0.001*
AI (median (Q1-Q3); e/h)	16.00 (7.6–30.0)	6 months	2.20 (0.9–3.7)	< 0.001*
		12 months	3.50 (1.1–5.5)	< 0.001*
Supine AHI (median (Q1-Q3); e/h)	59.30 (38.4–77.4)	6 months	22.60 (9.6–31.9)	0.001*
		12 months	20.70 (12.5–36.9)	< 0.001*
Non-supine AHI (median (Q1-Q3); e/h)	25.60 (15.3–27.2)	6 months	5.90 (2.3–12.4)	< 0.001*
		12 months	8.40 (2.7–11.3)	< 0.001*
ODI ≥ 3% (median (Q1-Q3); e/h)	32.90 (27.9–36.9)	6 months	11.60 (6.8–16.4)	< 0.001*
		12 months	14.30 (10.7–25.2)	< 0.001*
ODI ≥ 4% (median (Q1-Q3); e/h)	20.10 (16.5–27.2)	6 months	4.50 (1.7–7.4)	< 0.001*
		12 months	6.00 (5.0–12.6)	< 0.001*
Mean SpO2 (mean ± SD)	93.91 ± 1.30	6 months	94.08 ± 1.54	0.472**
		12 months	93.71 ± 1.70	0.346**
ESS (mean ± SD)	10.28 ± 5.26	6 months	7.95 ± 2.93	0.007**
		12 months	7.04 ± 3.61	0.002**
Therapy usage (mean ± SD; h/night)	–	6 months	6.96 ± 1.59	–
		12 months	5.83 ± 1.70	–

Abbreviations: AHI, apnea-hypopnea index; AI, apnea-index; BMI, body-mass index; ESS, Epworth sleepiness scale; ODI, oxygen desaturation index; Q1, quartile 1; Q3, quartile 3; SD, standard deviation, SpO2, arterial oxygen saturation.
*Wilcoxon signed-rank test
**Paired *t*-test

Table 3 Clinical global impression

Clinical global impression	6 months	12 months
Very much improved	6 (24%)	11 (47.83%)
Much improved	12 (48%)	8 (43.78%)
Minimally improved	6 (24%)	4 (17.39%)
No change	1 (4%)	0 (0%)
Minimally worse	0 (0%)	0 (0%)
Much worse	0 (0%)	0 (0%)
Very much worse	0 (0%)	0 (0%)

baseline AHI was 37.40 (33.7–45.6) e/h, with a mean ESS of 10.28 ± 5.26. The median ODI $\geq$ 4% was 20.10 (16.5–27.2) e/h. Fourteen patients (56%) previously underwent a tonsillectomy. All other patients had small tonsils, varying from tonsil size 1 to 2. The median Mallampati score was 3.

Objective Outcome Measures

A complete overview of the objective outcome measures at 6- and 12-month follow-up is shown in ►**Table 2**. The total median AHI at the 6-month follow-up significantly decreased from 37.40 (33.7–45.6) e/h to 8.10 (3.9–15.0) e/h ($p < 0.001$). Both the median AHI in supine position and non-supine position significantly decreased, from 59.30 (38.4–77.4) e/h to 22.60 (9.6–31.9) e/h and from 25.60 (15.3–27.2) e/h to 5.90 (2.3–12.4) e/h, respectively ($p = 0.001$; $p < 0.001$). The median ODI $\geq$ 4% significantly decreased from 20.10 (16.5–27.2) e/h to 4.50 (1.7–7.4) e/h ($p < 0.001$). The mean therapy usage at the 6-month follow-up was 6.96 ± 1.59 hour/night. The median AHI at 12-month follow-up significantly decreased to 8.70 (4.8–12.7) e/h ($p < 0.001$). The median AHI in supine position and non-supine position was 20.70 (12.5–36.9) e/h and 8.40 (2.7–11.3) e/h, respectively ($p < 0.001$; $p < 0.001$). The median ODI $\geq$ 4% was 6.00 (5.0–12.6) e/h ($p < 0.001$). The mean therapy usage at 12-month follow-up was 5.83 ± 1.70 hour/night.

Subjective Outcome Measures

The mean ESS significantly decreased from 10.28 ± 5.26 to 7.95 ± 2.93 and 7.04 ± 3.61 respectively at 6- and 12-month follow-up ($p = 0.007$; $p = 0.002$) (►**Table 2**). The summarized data of CGI at 6- and 12-month follow-up is shown in ►**Table 3**. At the 6-month follow-up, the CGI of 96% of the patients is minimally, much, or very much improved. At the 12-month follow-up, all patients were at least minimally improved in comparison to baseline. ►**Table 4** shows the

Table 4 Patient experience with therapy

Patient Experience with Therapy		6 months	12 months
How does your UAS therapy compare against your previous experience with CPAP?	UAS is much better than CPAP	76.92%	65.22%
	UAS is better than CPAP	7.69%	4.35%
	CPAP and UAS are equal	0%	0%
	CPAP is better than UAS	0%	4.35%
	CPAP is much better than UAS	0%	4.35%
	N/A – No experience with CPAP or did not use CPAP long enough	15.38%	21.74%
What is the likelihood of choosing UAS therapy again?	Strongly agree	84.62%	65.22%
	Agree	15.38%	17.39%
	Neither agree nor disagree	0%	8.7%
	Disagree	0%	4.35%
	Strongly disagree	0%	4.35%
What is the likelihood of recommending UAS therapy to friends/family?	Strongly agree	69.23%	43.48%
	Agree	15.38%	30.43%
	Neither agree nor disagree	15.38%	17.39%
	Disagree	0%	8.7%
	Strongly disagree	0%	0%
Overall, how satisfied are you with UAS therapy?	Very satisfied	38.46%	21.74%
	Satisfied	53.85%	47.83%
	Neither satisfied nor dissatisfied	7.69%	21.74%
	Dissatisfied	0%	4.35%
	Very dissatisfied	0%	4.35%

Abbreviations: CPAP, continuous positive airway pressure; UAS, upper airway stimulation.

results of the PET questionnaire. At the 6- and 12-month follow-ups, respectively, 84.61% and 69.57% of the patients declared UAS was better than CPAP therapy; 100% and 82.61% would choose UAS again; 84.61% and 73.91% would recommend UAS to friends/family; 92.31% and 69.57% were satisfied with UAS therapy.

Surgical Success

The surgical success rate according to the Sher criteria was 92% at the 6-month follow-up and 96% at the 12-month follow-up. Additionally, at the 6-month follow-up, 76% met the additional criteria of $\geq$ 50% reduction from baseline AHI and a postoperative AHI of $\leq$ 15. At the 12-month follow-up, 88% had met the additional criteria.

Adverse Events

A complete overview of reported AEs is presented in ►**Table 5**. Nine patients (36%) reported at least one adverse event at the 6-month follow-up. Ten AEs were reported in total, with stimulation-related discomfort being the most common, reported 7 times (28%). Two patients (8%) developed a submental hematoma postoperatively. One patient (4%) developed a postoperative wound infection. At the 12-month follow-up, 7 patients (28%) reported at least one AE, with a total of 8 AEs reported. Three patients (12%) still experienced stimulation-related discomfort. Two patients (8%) experienced tongue abrasion. One patient (4%) experienced dentofacial changes of the lower teeth, and two patients (8%) needed an additional barbed stitch

Table 5 Adverse events

Time point	Overall AE rate*	Adverse event	Frequency of AE reported				
			Total reported**	Frequency of AE***	Mild****	Moderate****	Severe****
6 Months	9 (36%)	Tongue weakness	10	0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Swallowing/speech related AE		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Discomfort related to incision/scar		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Discomfort related to IPG		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Infection		1 (4%)	1 (4%)	0 (0%)	0 (0%)
		Other procedure related AE±		2 (8%)	2 (8%)	0 (0%)	0 (0%)
		Stimulation related discomfort		7 (28%)	7 (28%)	0 (0%)	0 (0%)
		Tongue abrasion		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Insomnia/arousals		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Revision intervention		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Other therapy related AE		0 (0%)	0 (0%)	0 (0%)	0 (0%)
12 Months	7 (28%)	Tongue weakness	8	0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Swallowing/speech related AE		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Discomfort related to incision/scar		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Discomfort related to IPG		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Infection		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Other procedure related AE		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Stimulation related discomfort		3 (12%)	3 (12%)	0 (0%)	0 (0%)
		Tongue abrasion		2 (8%)	2 (8%)	0 (0%)	0 (0%)
		Insomnia/arousals		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Revision intervention		0 (0%)	0 (0%)	0 (0%)	0 (0%)
		Other therapy related AE±±		3 (12%)	3 (12%)	0 (0%)	0 (0%)

Abbreviations: AE, adverse event; IPG, implanted pulse generator.
*This number represents the total number of patients who reported at least one AE
**This number represents the total number of AEs reported at this time point
***This number represents the number and percent of patients who reported this AE
****This number represents the number and percent of patients who reported this AE with each severity of the AE reported
±Two patients developed a submental hematoma postoperatively.
±±One patient experienced dentofacial changes of the lower teeth, two patients needed an additional barbed reposition pharyngoplasty due to lack of palatoglossal coupling.

pharyngoplasty due to persistent velopharyngeal collapse as a result of lack of palatoglossal coupling.[11] No severe or irreversible AEs were reported.

Discussion

The present study aimed to retrospectively analyze the long-term postoperative outcomes of UAS in patients with moderate to severe OSA with CPAP failure or intolerance. Upper airway stimulation significantly improved respiratory parameters measured by PSG. The overall surgical success rate measured by the Sher criteria was 92% and 96% at the 6- and 12-month follow-ups, respectively. Additionally, there was a significant decrease in ESS measured at the 6- and 12-month follow-ups.

Thaler et al. recently published the results of 382 patients enrolled in the ADHERE upper airway registry.[10] They found a significant reduction in median AHI from 32.8 e/h to 6.3 e/h and 9.5 e/h at the 6- and 12-month follow-ups, respectively. The surgical success rate, according to the Sher criteria, was 85% and 69%, respectively. They found a significant reduction in the median ESS from 11.0 to 7.0 and 6.0, respectively. The mean therapy usage at 12-month follow-up was 5.7 hour/night. Ninety-two percent of investigators reported improvement with treatment after the participant received an UAS system; 93% of participants reported overall satisfaction with UAS treatment; 95% preferred UAS over CPAP; 94% would choose UAS again if asked; and 96% would recommend UAS to family and friends. Adverse events were reported by 46% at the 6-month follow-up and 32% at the 12-month follow-up. Previously, Heiser et al. also published results of the ADHERE upper airway registry.[9] Reporting on 508 patients, the median AHI decreased from 34.0 e/h to 5.7 e/h and 7.0 e/h, respectively, at the posttitration and the final follow-up visits. The surgical success rate, according to the Sher criteria, was 92% and 81%, respectively. The mean ESS decreased significantly from 11.8 to 7.7 and 6.7, respectively. Ninety-four percent of physicians rated improvement on the CGI, which persisted in 93% at the final visit. Ninety-six percent of the subjects reported that UAS was better than CPAP therapy post-titration and at the final follow-up visit; 95% stated that they would undergo UAS again at the post-titration visit; and 94% at the final follow-up visit. Ninety-three percent reported that they would recommend UAS to family and friends, which increased to 96% at the final follow-up visit. Ninety-one percent reported that, overall, they were satisfied with UAS therapy at the post-titration visit, and 94% at the final follow-up visit. Boon et al. also reported on the ADHERE upper airway registry and reported similar outcomes to those of Thaler et al. and Heiser et al.[7] Mehra et al. recently published a parallel arm study design to compare objective sleep apnea measures, and patients reported outcomes in those who received UAS approval versus denial in a multinational prospective study.[15] In 250 patients treated with UAS, they found a significant reduction in median AHI from 31.3 e/h to 10.1 e/h at the 12-month follow-up. There was a significant decrease in the mean ESS from 13.0 to 6.0. Freedom from procedure-related AEs was present in 97% of those who underwent UAS. Freedom of therapy-related AEs was present in 90%. Woodson et al. reported 5-year outcomes of patients receiving UAS therapy. They reported a surgical success measured by the Sher criteria of 75%. The responder rate at the 5-year follow-up was 63%.[8] Earlier, Strollo et al. found a significant reduction in AHI from 29.3 e/h to 9.0 e/h and ODI from 25.4 to 7.4 e/h in moderate-to-severe OSA patients 12-months after implantation, with a surgical success rate of 66%.[6] The mean ESS significantly decreased from 11.6 to 7.0.

In comparison to previously published studies, the baseline AHI was higher in our patient population. This can be explained by the fact that, in the Netherlands, costs for treatment with UAS are only reimbursed for patients with an AHI between 30 and 50 e/h, while in most other countries the inclusion range is 15 to 65 e/h. The postoperative AHI was similar to those of earlier studies, indicating that the reduction in AHI is larger than in previous studies. The surgical success rate according to the Sher criteria was also higher than in previous studies. The reduction in ESS and the CGI was similar to what was mentioned by previous authors. The answers to the PET questionnaire were less positive in this cohort in comparison to previous descriptions of larger cohorts. A possible explanation can be that the two patients who received an additional barbed reposition pharyngoplasty due to lack of palatoglossal coupling were dissatisfied due to the fact that they needed additional surgery. This has largely influenced the results due to the small sample size. The adverse event rate was similar to the AE rate mentioned by Thaler et al.[10] However, Mehra et al. reported a lower AE rate.[15] In this cohort, no severe or irreversible AEs were reported. Stimulation-related discomfort was the most common AE reported. This is generally a short-term problem, and most patients do not experience discomfort after an intensive titration period.

In the present cohort, the AHI in non-supine position showed a larger decrease in comparison to baseline than the AHI in supine position. A possible explanation for this is that in our experience during in-laboratory titration visits, in supine position a higher stimulation level is needed than in non-supine position. However, this stimulation level is often not tolerated by the patients, causing discomfort and waking them up at night, forcing them to lower the stimulation themselves. This is probably the reason why the AHI in non-supine position shows a larger decrease than the AHI in supine position.

It is notable that, at the 12-month follow-up, the success rate according to the Sher criteria was higher than the success rate at the 6-month follow-up. This indicates that long and intensive follow-up shows improvement of respiratory parameters. The ESS was also lower at the 12-month follow-up, indicating that patients experienced less OSA-related complaints. In contrast, the answers to the PET questionnaire were less positive at the 12-month follow-up. A possible explanation can be that the two patients who received an additional barbed reposition pharyngoplasty due to lack of palatoglossal coupling were dissatisfied due to the fact that they needed additional surgery. Preoperative screening measures are needed to identify patients without palatoglossal coupling. Additionally, not all patients are aware of the intensive titration that is needed in the first

year after implantation. Further counseling and intensive follow-up are needed to maintain favorable results.

Clinical Relevance

Obstructive sleep apnea is associated with cardiovascular and metabolic consequences and is also linked with increased overall mortality.[16] Therefore, in patients with moderate-to-severe OSA and CPAP failure or intolerance, alternative treatment options are important. In this patient cohort in the Netherlands, UAS shows a high surgical success rate with no severe or irreversible AEs. This is similar to the results of previous studies in other countries. Therefore, UAS is an effective and safe alternative in patients with CPAP failure or intolerance.

Limitations and Strengths

The present study is not without limitations. In the Netherlands, the inclusion criteria for UAS include a BMI $<$ 32, whereas, worldwide, the inclusion criteria range up to a BMI of 35. Additionally, patients with a complete concentric collapse at the velopharyngeal level were excluded. It is possible that this introduces a selection bias that has positively influenced our results. However, a complete concentric collapse at the velopharyngeal level is currently globally used as an exclusion criterion. Additionally, the results represent the experience of one center. The small sample size of this study is a limiting factor. The published series from Amsterdam, by Vonk et al., describes a larger cohort.[17] However, this is the first study conducted in the Netherlands that reports on long-term follow-up results. Additionally, both objective and subjective outcome measures are reported as well as therapy usage. All patients were followed-up with PSG, whereas, in previous studies reporting on the ADHERE registry, the AHI was based on both PSG and home sleep tests.

Conclusion

Upper airway stimulation proved to be a safe and effective treatment for OSA in patients with CPAP failure or intolerance, with a surgical success rate of 96%. Overall patient satisfaction was high, and no severe or irreversible AEs were reported. However, it is possible that the existing in and exclusion criteria for UAS therapy in the Netherlands have positively influenced our results.

Financial Support
There was no funding received for this research.

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 and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Data on study subjects was collected and stored anonymously to protect personal information. This manuscript does not report on a clinical trial and, therefore, was not registered in a clinical trial registration.

Manuscript Approval
All authors declare that they have seen and approved the final version of the manuscript.

Availability of Data and Materials
The dataset is available on request from St. Antonius Hospital, The Netherlands.

Conflict of Interests
The authors have no conflict of interests to declare.

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