Upper Airway Stimulation for OSA: Early Adherence and Outcome Results of One Center

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Abstract

Objective. To review outcome measures and objective adherence data for patients treated with hypoglossal nerve stimulation (HNS) therapy for moderate to severe obstructive sleep apnea (OSA).

Study Design. Case series with chart review.

Setting. Academic sleep medicine center.

Subjects and Methods. The first 20 implanted patients to complete postoperative sleep laboratory testing were assessed. All patients had moderate to severe OSA, were unable to adhere to positive pressure therapy, and met previously published inclusion criteria for the commercially available implantable HNS system. Data included demographics, body mass index (BMI), apnea-hypopnea index (AHI), Epworth Sleepiness Score (ESS), nightly hours of device usage, and procedure- and therapy-related complications.

Results. Mean age was 64.8 ± 12.0 years, with 50% female. Mean BMI was unchanged postoperatively (26.5 ± 4.2 to 26.8 ± 4.5 kg/m2; P > .05). Mean AHI (33.3 ± 13.0 to 5.1 ± 4.3; P < .0001) and mean ESS (10.3 ± 5.2 to 6.0 ± 4.4; P < .01) decreased significantly. Seventy percent (14/20) of patients achieved a treatment AHI < 5, 85% (17/20) an AHI < 10, and 95% (19/20) an AHI < 15. Average stimulation amplitude was 1.89 ± 0.50 V after titration. Adherence monitoring via device interrogation showed high rates of voluntary device use (mean 7.0 ± 2.2 h/night).

Conclusion. For a clinical and anatomical subset of patients with OSA, HNS therapy is associated with good objective adherence, low morbidity, and improved OSA outcome measures. Early results at one institution suggest that HNS therapy can be implemented successfully into routine clinical practice, outside of a trial setting.

Keywords

obstructive sleep apnea, upper airway stimulation, hypoglossal nerve stimulation, sleep surgery
Randomized therapy withdrawal for 1 week in a subset of these patients (n = 46) resulted in return of AHI, ESS, and FOSQ to baseline levels, but reactivation maintained therapeutic efficacy over a year later. More recent data in STAR trial participants have shown that improvement in outcome measures is maintained at 18 and 24 months with no functional impairment of the hypoglossal nerve.

The current report focuses on outcomes of HNS implantation as part of routine clinical practice, outside the context of a clinical research trial, at a single academic sleep center, which began after FDA approval of the implantable HNS system in April 2014.

**Methods**

This study was designed as a retrospective case series with chart review of 21 consecutive patients who underwent implantation at a single institution by a single surgeon (R.J.S.) between May 2014 and March 2015. This research was conducted under University of Pittsburgh Institutional Review Board–approved protocol PRO13030372.

**Patient Selection**

Patients were selected for HNS implantation by the senior author (R.J.S.) as part of routine clinical practice based on selection criteria previously established from the STAR trial. Qualified patients presented with a body mass index (BMI) ≤32 kg/m² and a diagnosis of moderate to severe OSA (central apnea index <25%) based on the most recent diagnostic polysomnography report. All patients were unable to adhere to PAP despite multiple attempts and mask refits.

Patients meeting the clinical, BMI, and sleep study inclusion criteria then underwent drug-induced sedation endoscopy (DISE) to evaluate the anatomical locations and pattern of collapse. Qualified patients demonstrated a primarily anterior-posterior pattern of pharyngeal collapse during DISE with evidence of mechanical coupling between the tongue and palate. Patients with a primary pattern of complete concentric palatal collapse with a large lateral oropharyngeal wall component were offered other forms of medical or surgical OSA treatment.

**Surgical Procedure**

The Inspire implantable HNS system (Inspire Medical Systems, Minneapolis, Minnesota) was implanted by the senior author (R.J.S.) in each patient in accordance with previously published surgical techniques. The surgical implantation procedure was performed as outpatient surgery at a single academic medical center, and all patients received preoperative antibiotics via one intravenous dose 30 to 60 minutes prior to skin incision. The HNS system consists of a stimulation cuff electrode on the distal branches of the hypoglossal nerve, an implantable pulse generator in the right upper chest, and a pleural respiratory sensor in the intercostal space.

The device consists of a neurostimulation pulse generator inserted into a subcutaneous pocket inferior to the right mid-clavicle. The generator is connected to an intercostal respiratory pressure sensor in the right chest wall and a stimulation cuff electrode on the right hypoglossal nerve. Intraoperative nerve monitoring and visualization of tongue movement were used to identify and selectively include branches of the hypoglossal nerve to the genioglossus muscle in the stimulation cuff electrode to generate tongue protrusion (Figure 1). Retractor branches of the hypoglossal nerve to the styloglossus and hyoglossus muscles were excluded. If anatomically feasible, the hypoglossal nerve branch to the geniohyoid muscle was also included in the stimulation cuff electrode.

**Postoperative Care and Management**

All patients were discharged to home with recommendations for regular diet and over-the-counter acetaminophen or ibuprofen as needed for incisional discomfort in the immediate postoperative period. Patients were advised to avoid vigorous or repetitive activity of the right arm for 2 to 3 weeks postoperatively. Clinical follow-up after device implantation included a postoperative examination within 1 to 2 weeks, device activation and initiation of therapy 1 month after implantation, and follow-up polysomnography testing and clinical assessment 2 to 6 months after implantation (Figure 2).

**Data Collection and Statistical Analysis**

Data collected from the chart review included age, sex, pre- and postoperative BMI, history of OSA treatment, and any procedure- and therapy-related complications. Self-reported data consisted of pre- and postoperative ESS. Mean nightly hours of therapy use were obtained through device interrogation during routine outpatient follow-up. Sleep study data collected...
included pre- and postoperative AHI and lowest oxygen saturation (LSAT). Nonparametric 2-tailed Wilcoxon signed-rank tests at a significance level of $P < .05$ were used to compare all variables in Stata (release 14; StataCorp LP, College Station, Texas).

**Results**

Twenty-one patients underwent HNS implantation between May 2014 and March 2015. One patient had not completed postoperative polysomnography by the time of data analysis and manuscript submission and was therefore excluded from data analysis. Of the remaining 20 patients, 50% (n = 10) were male and 50% (n = 10) were female (Table 1). Mean age was 64.8 ± 12.0 years, mean BMI was 26.5 ± 4.2 kg/m², mean ESS was 10.3 ± 5.2, and mean AHI was 33.3 ± 13.0 prior to HNS implantation.

In addition to inadequate PAP adherence, 55% (11/20) also had prior intolerance or inadequate effectiveness with oral appliance therapy (Table 2). Fifty percent (10/20) had previously undergone upper airway reconstructive surgery, including uvulopalatopharyngoplasty, genioglossus advancement, hyoid suspension, expansion pharyngoplasty, and functional nasal surgery. Cumulatively, 35% (7/20) failed to achieve adequate benefit with both oral appliance therapy and upper airway reconstructive surgery.

Mean postoperative sleep laboratory testing was completed 91.4 ± 45.4 days (range, 58-222 days) after HNS implantation. Mean interval from HNS implantation to most recent office visit was 232.6 ± 101.9 days (range, 109-400 days). The variability in clinical follow-up was primarily a manifestation of the month and year the implant was performed, as patients implanted earlier had a longer course of postoperative evaluation.

Mean BMI did not change significantly from baseline to postoperative follow-up (26.5 ± 4.2 to 26.8 ± 4.5 kg/m²; $P > .05$). Mean ESS (10.3 ± 5.2 to 6.0 ± 4.4; $P < .01$) and mean AHI (33.3 ± 13.0 to 5.1 ± 4.3; $P < .0001$) were significantly reduced postoperatively (Figures 3 and 4). Of the 20 patients, 70% (14/20) achieved a treatment AHI < 5, 85% (17/20) an AHI < 10, and 95% (19/20) an AHI < 15. The 1 patient (1/20) without good clinical response (AHI > 15) also had poor tongue movement with stimulation, demonstrating mixed coactivation of both retractor and protrusor muscles. The other 19 of 20 responders demonstrated good bilateral tongue protrusion with activated therapy. The significant improvement in mean AHI is due to large decreases in AHI across the majority of the study cohort as opposed to normalization of outlier subjects, as would be expected in regression to the mean (Figure 5).

The LSAT was not significantly different during preoperative and postoperative sleep study (79.8% ± 6.8% to 82.2% ± 5.2%; $P > .05$). Time spent below 90% oxygen saturation was also not significantly different between pre- and postoperative sleep studies (15.5 ± 21.4 to 14.1 ± 22.0 minutes). Average stimulation amplitude was 1.89 ± 0.50 V after device titration. Objective adherence monitoring via device interrogation was available on all patients and showed high rates of voluntary device use (mean 7.0 ± 2.2 h/night) over the time course of clinical follow-up above. Objective device data for 1 patient were not available at the time of manuscript submission as further postoperative clinic assessment had been deferred due to a new cancer diagnosis requiring frequent chemotherapy treatments.

Two patients experienced postoperative seroma at an incision site in the immediate postoperative period, and 1 patient experienced prolonged incisional discomfort. One seroma occurred at the sensing lead incision 1 week after surgery and the other at the implantable pulse generator incision 4 weeks after surgery. Both resolved uneventfully.

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**Table 1. Preoperative Characteristics of 20 Patients Undergoing Hypoglossal Nerve Stimulation Implantation.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>64.8 ± 12.0</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>1:1</td>
</tr>
<tr>
<td>White/other race ratio</td>
<td>19:1</td>
</tr>
<tr>
<td>BMI, mean ± SD, kg/m²</td>
<td>26.5 ± 4.2</td>
</tr>
<tr>
<td>AHI, mean ± SD</td>
<td>33.3 ± 13.0</td>
</tr>
<tr>
<td>T90, mean ± SD, min</td>
<td>15.5 ± 21.4</td>
</tr>
<tr>
<td>ESS, mean ± SD</td>
<td>10.3 ± 5.2</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; T90, time with oxygen saturation <90%.
with in-office percutaneous needle drainage. There were no postoperative wound infections, no subjective change in speech or swallowing, and no weakness of the hypoglossal or marginal mandibular nerves on postoperative examinations. The patient with prolonged incisional discomfort reported 6 weeks of pain at the sensing lead site when lying on the right side that required prescription of opioid pain medication. Therapy-related side effects included 3 patients reporting dry mouth in the morning and 1 patient reporting mild tongue abrasion after device activation due to the tongue rubbing against the maxillary teeth during protrusion, which spontaneously resolved.

**Discussion**

Implantation of HNS resulted in significant improvements in the primary objective metric of OSA disease severity as well as self-reported sleepiness in a group of patients presenting to one academic sleep center as part of routine clinical practice. Seventy percent of the patients in our cohort demonstrated an AHI reduction with therapy from the moderate to severe range into the normal range (AHI <5), and 95% were reduced to an AHI <15. Interestingly, the only patient with persistent AHI elevation over 15 was also the only patient with poor tongue protrusion during stimulation and is scheduled for revision electrode placement at the time of manuscript submission. No serious adverse events were observed, and minor side effects were either easily managed in the outpatient clinic setting or resolved spontaneously. Therapy acceptance and adherence were high, as demonstrated by objective device interrogation.

### Table 2. Attempted OSA Medical and Surgical Treatments Prior to Undergoing HNS Implantation and Breakdown of Individual Objective and Subjective Outcome Measures.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Prior OSA Medical Therapy</th>
<th>Prior OSA Surgical Therapy</th>
<th>AHI Preoperative</th>
<th>AHI Postoperative</th>
<th>ESS Preoperative</th>
<th>ESS Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CPAP, OAT</td>
<td>UPPP, GGA, HMS</td>
<td>45</td>
<td>3.7</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>CPAP, OAT</td>
<td>None</td>
<td>64.0</td>
<td>7.8</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>CPAP, OAT</td>
<td>NS</td>
<td>20.2</td>
<td>2.2</td>
<td>15</td>
<td>10</td>
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<tr>
<td>4</td>
<td>CPAP, OAT</td>
<td>None</td>
<td>39.5</td>
<td>3.2</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>CPAP, BiPAP, OAT</td>
<td>NS, ESP</td>
<td>42.0</td>
<td>3.5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>CPAP</td>
<td>UPPP</td>
<td>39.6</td>
<td>3.0</td>
<td>16</td>
<td>9</td>
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<tr>
<td>7</td>
<td>CPAP, auto-BiPAP</td>
<td>NS</td>
<td>41.6</td>
<td>10.7</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>BiPAP</td>
<td>None</td>
<td>30.0</td>
<td>4.8</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>CPAP, OAT</td>
<td>NS</td>
<td>18.3</td>
<td>0.9</td>
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<td>4</td>
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<tr>
<td>10</td>
<td>CPAP</td>
<td>None</td>
<td>38.5</td>
<td>9.0</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>CPAP, OAT</td>
<td>UPPP, GGA, HMS</td>
<td>28.3</td>
<td>18.0</td>
<td>18</td>
<td>18</td>
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<tr>
<td>12</td>
<td>CPAP, OAT</td>
<td>None</td>
<td>26.9</td>
<td>1.6</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>13</td>
<td>CPAP, BiPAP, auto-BiPAP, OAT</td>
<td>NS, UPPP</td>
<td>35.8</td>
<td>1.4</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>14</td>
<td>CPAP, BiPAP</td>
<td>NS, UPPP</td>
<td>52.0</td>
<td>10.4</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>15</td>
<td>CPAP, OAT</td>
<td>NS, ESP</td>
<td>19.0</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16</td>
<td>CPAP</td>
<td>None</td>
<td>24.7</td>
<td>2.8</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>17</td>
<td>CPAP, auto-CPAP, OAT</td>
<td>None</td>
<td>18.2</td>
<td>4.0</td>
<td>8</td>
<td>4</td>
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<tr>
<td>18</td>
<td>CPAP, BiPAP</td>
<td>None</td>
<td>18.1</td>
<td>4.7</td>
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<td>5</td>
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<tr>
<td>19</td>
<td>CPAP</td>
<td>None</td>
<td>44.2</td>
<td>7.0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>CPAP</td>
<td>None</td>
<td>19.8</td>
<td>3.2</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

**Abbreviations:** AHI, apnea-hypopnea index; BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; ESP, expansion sphincter pharyngoplasty; ESS, Epworth Sleepiness Score; GGA, genioglossus advancement; HMS, hyoid myotomy and suspension; HNS, hypoglossal nerve stimulation; NS, nasal surgery; OAT, oral appliance therapy; OSA, obstructive sleep apnea; UPPP, uvulopalatopharyngoplasty.
Previously published reports have documented the efficacy of HNS in a large prospective multicenter trial; however, the results of a motivated group of study participants do not necessarily translate into successful implementation in routine clinical practice. This is the first report of HNS outcomes in patients from an academic sleep medicine practice outside the context of a clinical trial. Although this study is limited by a small population and lack of a control group, our results suggest that thoughtful and conservative implementation of HNS into a multidisciplinary sleep practice can actually produce results that exceed those from past clinical trials. We hypothesize that subtle refinements in patient selection, upper airway evaluation via DISE, surgical technique, stimulation cuff electrode placement, therapy programming, and therapy titration are likely responsible for further improved outcomes.

Positive airway pressure remains the standard first-line therapy for the management of moderate to severe OSA, but nonacceptance or inadequate adherence remains a significant challenge that often necessitates the exploration of alternative treatment modalities. Our reported success rates, based on objective outcome measures and objective adherence monitoring, are high in a cohort of patients previously intolerant of PAP. Hypoglossal nerve stimulation is currently considered second-line therapy, and all patients being considered for implantation at our center must have previously demonstrated thorough efforts to make PAP therapy successful. In our academic sleep medicine and surgery practice, PAP intolerance is a common complaint. Our patients undergo PAP mask refits, pressure or therapeutic mode adjustments, repeat PAP titrations, disease and therapy education, and close clinical follow-up with objective data card monitoring before being considered for alternative treatment strategies.

Second-line PAP alternatives may include oral appliance therapy, positional therapy, weight loss, lowering of nasal resistance, and surgical alteration of the upper airway. Oral appliance therapy currently has the most robust safety and effectiveness data of all second-line options, and most of our patients with adequate dentition are recommended a trial of an oral appliance after initial PAP failure. However, at least half of patients with moderate to severe OSA are not sufficiently treated with an oral appliance alone. Others are not candidates due to lack of adequate dentition or lack of insurance coverage, or they discontinue therapy due to discomfort, occlusal change, or other side effects. In our cohort, 55% of patients attempted oral appliance therapy but discontinued it due to inadequate effectivity or adverse side effects. The other 45% were edentulous, nonaccepting of oral appliance risks, or deemed poor oral appliance candidates by the sleep dentist because of bone loss, unstable dentition, bridge work, or temporomandibular joint conditions.

Half of our patient cohort had previously undergone prior upper airway surgery before presenting to our center. Although this study was not designed to directly assess postoperative pain and complication rates between HNS and traditional upper airway surgeries, our HNS patient population reported substantially lower pain and recovery time after HNS implantation compared with our experience with anatomy-altering procedures, which is consistent with recently published postoperative pain visual analog scale data from the STAR trial. In our center, HNS implantation was performed as outpatient surgery with immediate resumption of normal diet, and most HNS patients reported only mild incisional discomfort for the first few days postoperatively, requiring either nonprescription analgesics or no pain medication at all. This postoperative course differs from our experience with pharyngeal and skeletal OSA surgery where overnight observation, need for opioid pain medication, dietary and swallowing changes, and increased time off work are more typical. In addition to the favorable effectiveness data, the minimal postoperative pain and morbidity may provide support for the use of HNS over airway surgery in some populations, such as the elderly or those with other medical comorbidities.

Two patients who were initially excluded from HNS consideration due to a complete concentric pattern of velopharyngeal collapse on DISE underwent expansion sphincter pharyngoplasty (ESP) to address the large lateral pharyngeal wall component. This resulted in partial subjective and

![Figure 4. Pre- and postoperative ESS. Mean ESS 10.3 ± 5.2 to 6.0 ± 4.4; P < .01. ESS, Epworth Sleepiness Scale.](image1)

![Figure 5. Pre- and postoperative AHI values decreased across the entire cohort. The dashed line represents the 1 subject with a mixed-activation pattern during therapy activation. AHI, apnea-hypopnea index.](image2)
objective improvement, but both patients had residual symptoms and persistent moderate to severe OSA documented on a postoperative sleep study. Both patients were found to have primarily anterior-posterior patterns of velopharyngeal collapse during subsequent DISE examination and were then successfully managed with HNS (final AHI <5). Our experience suggests that multimodality therapy may have value even with HNS therapy, but further study is required.

Conclusions
Hypoglossal nerve stimulation therapy is associated with excellent objective voluntary adherence, low morbidity, and significantly improved subjective and objective OSA outcome measures. Early clinical results at one institution suggest that the treatment can be implemented successfully into routine clinical practice outside of a clinical trial setting.

Author Contributions
David T. Kent, data collection, interpretation, writing, revising; Jake J. Lee, data collection, interpretation, writing, revising; Patrick J. Strollo Jr., data interpretation, revising; Ryan J. Soose, design, data collection, analysis, interpretation, writing, revising, final approval.

Disclosures
Competing interests: Ryan J. Soose is a consultant for Inspire Medical Systems and has provided research support as an investigator in the STAR trial. Patrick Strollo is a study investigator for Inspire Medical Systems; is on the scientific advisory board and has received grant support from ResMed; is on the scientific advisory board of Jazz Pharmaceuticals; is a consultant for Emmi Solutions, PinMed, and the National Football League; and has received grant support from Philips Respironics and the National Institutes of Health.

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References