

CORRESPONDENCE: OUR EXPERIENCE

Improved exposure of the hypoglossal branches during hypoglossal nerve stimulator implantation: Clinical outcomes of twenty patients at a single institution

1 | INTRODUCTION

Obstructive sleep apnoea (OSA) is a sleep disorder caused by complete or partial obstruction of the upper airway causing episodes of apnoea. Untreated OSA is associated with increased risk of and worsening of hypertension, cardiovascular disease and metabolic abnormalities. The standard of care for treatment of OSA is continuous positive airway pressure (CPAP). However, approximately 50% report inability to achieve long-term adherence to CPAP.¹

Hypoglossal nerve stimulation (HNS) for the treatment of moderate to severe OSA in adults was approved by the Food and Drug Administration in April, 2014. HNS has been shown to significantly improve respiratory events and as an effective second-line treatment for patients who were intolerant or unable to obtain benefit from CPAP.^{2,3} The Stimulation Treatment for Apnea Reduction (STAR) trial proved the effectiveness of HNS in a prospective multicentre trial followed by a randomized therapy withdrawal trial.⁴ In this manuscript, we report outcomes for 20 patients who underwent HNS at our institution using a modification of the previously described surgical technique with superior identification of the distal hypoglossal nerve.⁵

2 | MATERIALS AND METHODS

2.1 | Patient selection

The retrospective study examined 20 patients with OSA who underwent placement of HNS at one institution under a single surgeon. The study was approved by our institutional review board. Implantation dates were from December 2015 to April 2017. Criteria for implantation included patients with moderate to severe OSA (apnoea-hypopnea index (AHI) >15 and <65) who could not tolerate CPAP treatment. Patients were excluded if there was significant central or mixed apnea (>25%). Pre-operative work-up also included completing the Epworth Sleepiness Scale (ESS), home or inpatient polysomnography (PSG) and a drug-induced sleep endoscopy (DISE).

2.2 | Surgical implantation

Patients who met the implant criteria underwent placement of the Inspire implantable HNS system (Inspire Medical Systems, Maple Grove, MN). A modification of the previously described technique is

used to improve exposure of the distal hypoglossal nerve.⁵ The hypoglossal nerve is dissected anteriorly in the standard fashion. Next, the mylohyoid muscle is retracted off the hypoglossal nerve and approximately 2.0 cm of the posterior mylohyoid muscle is transected to improve exposure to the distal hypoglossal nerve (Figure 1A). A self-retaining retractor is placed under the digastric tendon and mandible ramus to facilitate exposure and dissection of the distal nerve (Figure 1B). A nerve integrity monitoring (NIM) system is used for precise selection of branches to be included in the cuff electrode. A bipolar nerve stimulator is used to help differentiate protractor (inclusion) branches from retractor (exclusion) branches. The cuff of the implantable pulse generator device is placed around all inclusion branches, which included the first cervical nerve (C1) branch to geniohyoid if possible (Figure 1C).

2.3 | Post-operative evaluation

The patients were seen post-operatively at 1 week and at routine intervals. The Inspire implants were activated 4-5 weeks following implantation. A post-operative PSG was performed at 8-9 weeks post-operatively. Post-operative evaluation of self-reported sleepiness was done through repeat ESS. Adverse events and complications were recorded and defined as serious events leading to death, life-threatening illness, hospitalisation, health impairment or need for operative intervention.

2.4 | Data collection

We examined medical records through the institution's electronic medical records system. Patient characteristics including age, gender, pre- and post-operative BMI were collected. Self-reported sleepiness was quantified through a pre- and post-implant ESS. Operative record was examined to obtain operative times and intraoperative complications. PSGs were conducted according to the American Academy of Sleep Medicine (AASM) guidelines. The patients were also called to complete the Patient Experience with Therapy (PET) questions obtained from the ADHERE Registry.⁶

2.5 | Statistical analysis

The pre-operative and post-operative outcome measures were compared. For the main outcomes, a paired *t* test was performed at a

5% significance level unless the normality assumption was violated, in that case a Wilcoxon test for paired samples was performed at the same significance level. The differences between gender were analysed using a two-sample Welch's *t* test. *P* values ≤ 0.05 were considered statistically significant. The analysis was made on R Statistical Software (Version 3.4.0).

3 | RESULTS

3.1 | Pre-implant characteristics

The study population consisted of 20 subjects. 70% were male, with a mean age of 58 years (range, 34-77 years-old), a mean BMI of 30 kg/m² (range, 23 to 38.5 kg/m²). All the subjects had a diagnosis of moderate to severe OSA (AHI range, 15-58) and had a history of CPAP non-compliance. Mean value for AHI score was 32 events/hour, oxygen desaturation index (ODI) score was 26.5 events/hour, ESS was 10.9 points, mean oxyhemoglobin saturation (SpO₂) percentage was 93.3%, minimum SpO₂ percentage was 81.4%, percentage less than 90% SpO₂ was 3.8%.

3.2 | Surgical implantation

The device was implanted successfully in all 20 subjects, with a mean surgical implant time of 115 minutes (range, 88-150 minutes). One patient had an immediate post-operative neck haematoma. One temporary marginal mandibular weakness was observed. None of the patients had any temporary or permanent hypoglossal nerve weakness.

Keypoints

- This retrospective study examined 20 patients who underwent hypoglossal nerve stimulation implantation for treatment of obstructive sleep apnea at a single institution.
- We utilised a modification in standard surgical technique allowing improved visualisation of the distal hypoglossal nerve.
- Main outcome and measures included apnea-hypoxia index, oxygen desaturation index, mean and minimum saturation and percentage of time below 90% saturation. We examined operative time and adverse events. Epworth Sleepiness Score and post-operative questionnaires were used to assess subjective measures of outcome.
- Our outcomes favourably compare to previously reported HNS outcomes and highlights the importance of optimal visualisation of the hypoglossal nerve distal branches.

3.3 | Post-implant characteristics

Compared to the baseline values (*n* = 20), the mean AHI score decreased by 94%, with a mean decrease of 30.2 events/hour (95% CI 24.9, 35.5) (Figure 2A). A total of 18 patients had an AHI less than 5 events/hour and two patients with AHI less than 15 events/hour. The median ODI score decreased 65% with a difference of the medians of

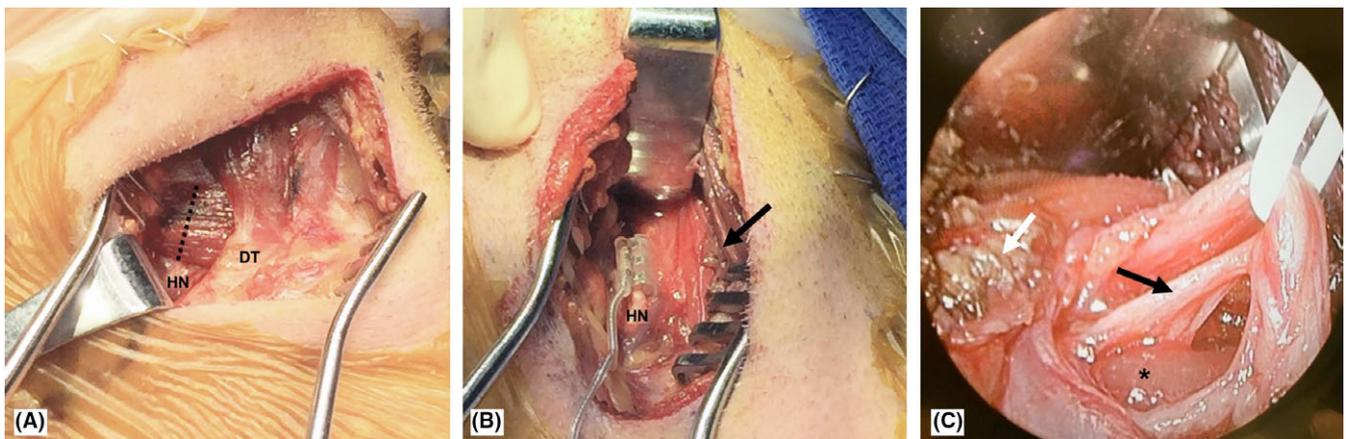


FIGURE 1 Dissection of the hypoglossal nerve and cuff placement. (a) The posterior border of the mylohyoid, the digastric tendon and the hypoglossal nerve are dissected out. Rather than operating through a tunnel, approximately 2 cm of the mylohyoid muscle are transected in order to improve the exposure of the distal hypoglossal nerve and facilitate cuff placement (HN=hypoglossal nerve; DT=digastric tendon; dotted line = extend mylohyoid split). (b) A self-retaining retractor is engaged under the digastric tendon, the previously split mylohyoid muscle and the mandibular ramus to avoid injury to the marginal mandibular nerve. Direct visualisation of distal nerve branches is easily possible. (arrow = digastric tendon and transected mylohyoid muscle retracted). (c) The improved exposure allows the surgeon to dissect the distal nerve branches efficiently and ensures identification of possible hidden exclusion nerve branches easily that are sometimes difficult to identify with nerve integrity monitoring (NIM) nerve mapping ensuring placement of the stimulation cuff only around protractor branches (vessel loop around inclusion branches; black arrow = "late take off branch"; asterisk = anterior border of hypoglossal muscle)

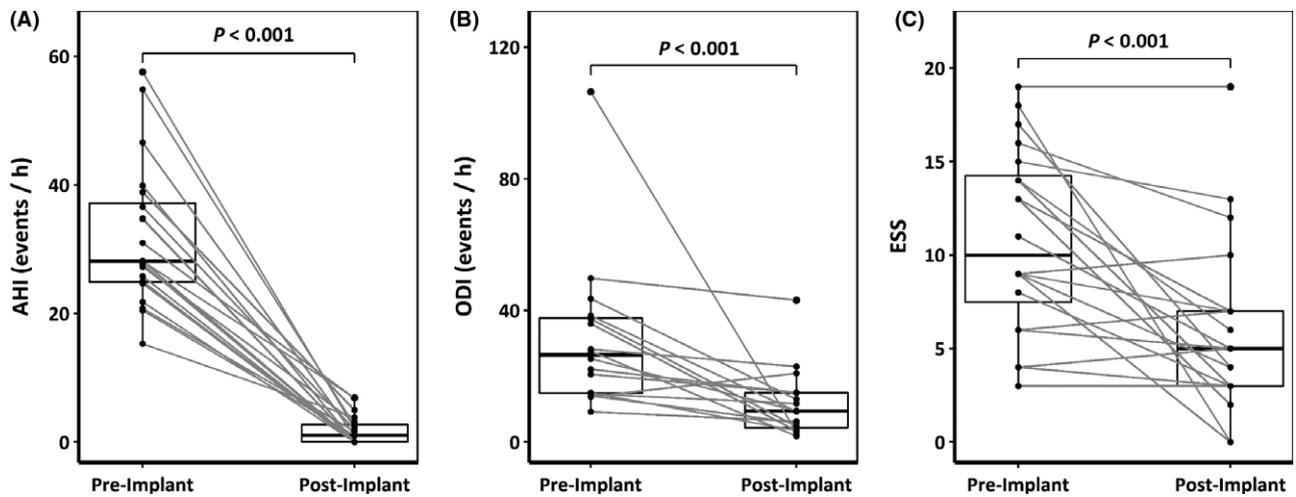


FIGURE 2 Box and whisker plot of (a) apnea-hypoxia index (AHI), (b) oxygen desaturation index (ODI) and (c) Epworth Sleepiness Score (ESS) pre-implant and post-implant. The median values are noted by the horizontal line within the box, and the boxes represent the intraquartile range. The whiskers represent the $1.5 \times$ the intraquartile range. The grey lines between the pre-implant and post-implant plot identifies the change in each individual patient

TABLE 1 Outcome measures

Outcome	Baseline	Post-implant PSG	Difference and 95% confidence interval (CI)	P value
AHI (Events/h), n = 20				
Mean (SD)	32 (11.22)	1.8 (2.27)		
T-test			30.2 (24.9, 35.5)	<0.001
ODI (Events/h), n = 16				
Median (IQR)	26.5 (22.73)	9.4 (10.63)		
Wilcoxon Test			16.5 (6.30, 27.45)	<0.001
ESS, n = 20				
Mean (SD)	10.9 (4.9)	5.9 (4.6)		
T-test			4.9 (2.45, 7.45)	<0.001
Mean SpO ₂ , n = 20				
Mean (SD)	93.3 (1.9)	92.9 (1.42)		
T-test			0.5 (−0.56, 1.46)	0.364
Minimum SpO ₂ , n = 20				
Mean (SD)	81.4 (5.46)	84.9 (3.8)		
T-test			−3.5 (−6.81, −0.29)	0.034
BMI (kg/m ²), n = 20				
Mean (SD)	30 (3.8)	30 (4.4)		
T-test			−0.01 (−1.22, 1.20)	0.986
Percentage of sleep <90% SpO ₂ , n = 18				
Mean (SD)	3.8 (5.3)	3.1 (6.6)		
T-test			0.7 (−0.63, 2.08)	0.276

16.5 events/hour (95% CI 6.3, 27.45) (Figure 2B). The minimum SpO₂ had a slight increase of 4.3% with a mean difference of −3.5% (95% CI −6.81, −0.29). There was no statistically significant difference in mean BMI, mean SpO₂ percentage and percentage of time below 90% saturation (Table 1). The mean pre-implant and post-implant AHI

difference for females was 27.9 and 31.2 for males. There was no significance difference between gender improvement (95% CI −15.24, 8.65). The mean time from implant to last follow-up PSG was 3.8 months (range, 1.9 to 14.6 months). The mean subjects' HNS usage time was 46 hours/week (range, 16-70 hours/week).

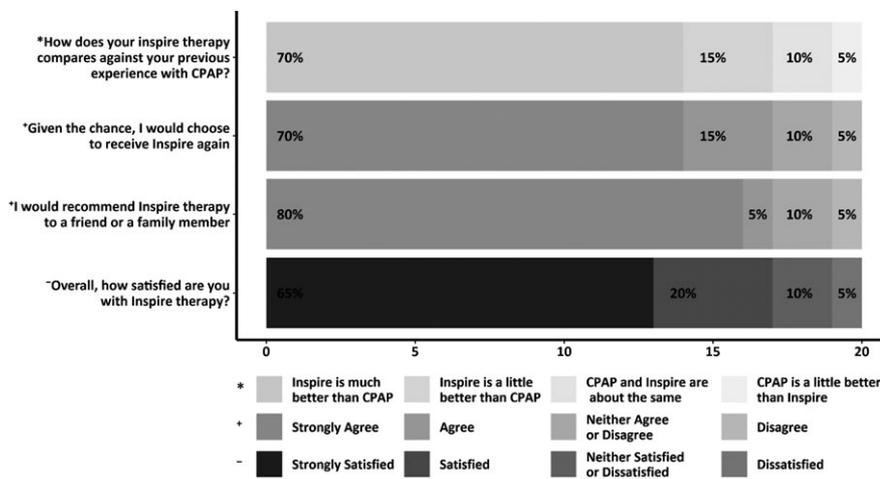


FIGURE 3 Results of the Patient Experience with Therapy (PET) questions obtained from the ADHERE Registry

3.4 | Post-implant subjective characteristics

The post-implant ESS and PET questionnaire were performed in all 20 subjects. There was a statistically significant decrease in ESS score by 4.9 (95% CI 2.45, 7.45) with a mean ESS of 6 following implantation (Figure 2C). The results from the PET can be seen in Figure 3.

4 | DISCUSSION

HNS is effective in treating patients with moderate to severe OSA as demonstrated in the STAR trial.^{2,4} Analysis of the outcomes for our 20 patients shows a dramatic improvement in quantitative measures of OSA. In our patients, the mean AHI score decreased by 94% from an average AHI of 32 to 1.8 events/hour. In a 3-year outcomes follow-up for the STAR trial, AHI was reduced from the median value of 28.2 events/hour to 8.7 and 6.2 events/hour at 12 and 36 months, respectively. A meta-analysis of 6 prospective studies of OSA patients who underwent HNS showed overall reduction in AHI between 50 to 57% and ODI reduction between 48 and 52%.⁷ In our series, ODI score decreased 65% with an average ODI of 26.45 prior to implantation to 9.4 events/hour. In addition to quantitative PSG results, our study demonstrated subjective improvement in OSA through improvement in ESS and positive response through the patient experience questionnaire.

The hypoglossal nerve innervates multiple muscles of the tongue including the retractors (styloglossus, hyoglossus), protrusors (genioglossus, horizontal and oblique) and stiffeners (transverse and vertical).^{8,9} There are reports of the utility of nerve monitoring to create a more selective upper-airway stimulation system by separating the inclusion and exclusion branches.^{5,10} Neuromonitoring leads placed in the hyoglossus and genioglossus muscle aid in stimulation cuff placement exclusively around the branches supplying tongue protractors. When stimulating the distal hypoglossal nerve, larger compound muscle action potentials from the transverse and oblique genioglossus muscles can mask the smaller hyoglossus muscle action

potentials giving a false sense of security when placing the cuff. Knowledge of distal hypoglossal nerve anatomy, in particular anterior to the hyoglossus muscle, is crucial to consistently identify small hypoglossal muscle nerve branches. These branches can be embedded in the main nerve, and therefore easily overlooked, especially when they course beyond the anterior border of the hyoglossus muscle prior to arcing superiorly from the distal main trunk. By partially splitting the mylohyoid muscle, the exposure to the distal hypoglossal nerve becomes significantly easier, avoiding distal hypoglossal nerve dissection through a “tunnel”. This superior exposure allows the surgeon to visualise these, at times, very small and embedded exclusion branches rather than solely trusting the NIMS signals. This approach allows for consistently correct cuff placement and selective protractor muscle stimulation. Further, the improved exposure may reduce the amount of hypoglossal nerve manipulation needed for cuff placement reducing the risk for stretch injury. None of the patients in our series had any post-operative tongue weakness.

5 | CONCLUSION

There are limitations in our study including the lack of a control comparison between patients who underwent the traditional surgical approach compared to our approach. Despite this, our clinical outcomes are comparable to previously reported outcomes of HNS. Our study provides further evidence regarding the safety and efficacy of HNS for OSA and highlights the importance of exposure of the distal hypoglossal nerve for optimising therapeutic outcome.

CONFLICT OF INTERESTS

There are no conflict of interests or financial disclosures to report.

ORCID

Akina Tamaki  <http://orcid.org/0000-0002-5603-1434>

Mark Weidenbecher¹

Akina Tamaki² 

Claudia Cabrera²

Kingman Strohl³

¹Department of Otolaryngology-Head and Neck Surgery, MetroHealth Hospital, Cleveland, Ohio

²Department of Otolaryngology-Head and Neck Surgery, University Hospitals Cleveland Medical Center, Cleveland, Ohio

³Division of Pulmonary, Critical Care and Sleep Medicine, University Hospitals Cleveland Medical Center, Cleveland, Ohio

Correspondence

Mark Weidenbecher, Department of Otolaryngology-Head and Neck Surgery, MetroHealth Hospital, Cleveland, OH.

Email: m.weidenbecher@metrohealth.org

REFERENCES

1. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *Lancet*. 2014;383(9918):736-747.
2. Woodson BT, Soose RJ, Gillespie MB, et al. Three-year outcomes of cranial nerve stimulation for obstructive sleep apnea: the STAR trial. *Otolaryngol Head Neck Surg*. 2016;154(1):181-188.
3. Malhotra A. Hypoglossal-nerve stimulation for obstructive sleep apnea. *N Engl J Med*. 2014;370(2):170-171.
4. Strollo PJ, Soose RJ, Maurer JT, et al. Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med*. 2014;370(2):139-149.
5. Heiser C, Thaler E, Soose RJ, Woodson BT, Boon M. Technical tips during implantation of selective upper airway stimulation. *Laryngoscope*. 2018;128(3):756-762.
6. Doghramji K, Heiser C, Schwab R, Strollo P. Patient outcomes and therapy adherence of upper airway stimulation for treatment of OSA: preliminary results from the multi center ADHERE registry. *Sleep*. 2017;40:A214.
7. Certal VF, Zaghi S, Riaz M, et al. Hypoglossal nerve stimulation in the treatment of obstructive sleep apnea: a systematic review and meta-analysis. *Laryngoscope*. 2015;125(5):1254-1264.
8. Oliven A, Tov N, Geitini L, et al. Effect of genioglossus contraction on pharyngeal lumen and airflow in sleep apnoea patients. *Eur Respir J*. 2007;30(4):748-758.
9. Mu L, Sanders I. Human tongue neuroanatomy: nerve supply and motor endplates. *Clin Anat*. 2010;23(7):777-791.
10. Heiser C, Hofauer B, Lozier L, Woodson BT, Stark T. Nerve monitoring-guided selective hypoglossal nerve stimulation in obstructive sleep apnea patients. *Laryngoscope*. 2016;126(12):2852-2858.