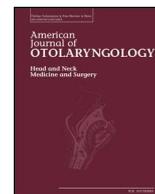




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Uvulopalatopharyngoplasty vs CN XII stimulation for treatment of obstructive sleep apnea: A single institution experience

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ABSTRACT

Objectives: Hypoglossal nerve stimulation (HNS) therapy is an emerging surgical treatment for select patients with obstructive sleep apnea (OSA). This study aims to compare outcomes in patients with moderate to severe OSA who underwent HNS surgery (Inspire Medical Systems) and those who underwent traditional airway reconstructive surgery, specifically uvulopalatopharyngoplasty (UPPP).

Methods: Patients who underwent HNS implantation (n = 20), all with moderate to severe OSA, inability to adhere to positive pressure therapy, and compliant with previously published inclusion criteria, were compared to a historical cohort that were intolerant of CPAP with similar inclusion criteria who all underwent UPPP (n = 20) with some also undergoing additional procedures such as septoplasty/turbinate reduction. Data including body mass index (BMI), pre- and post-implant apnea-hypopnea index (AHI) were assessed.

Results: For patients who underwent HNS, mean preoperative BMI was 28.0. Mean AHI decreased significantly from 38.9 ± 12.5 to 4.5 ± 4.8 . All patients achieved an AHI < 20 post implant with 65% (13/20) with an AHI ≤ 5 . For patients who underwent traditional airway surgery, mean preoperative BMI was 27.5; mean AHI decreased from 40.3 ± 12.4 to 28.8 ± 25.4 .

Conclusion: While both traditional surgery and HNS are effective treatments for patients with moderate to severe OSA with CPAP intolerance, our study demonstrates that HNS is “curative” in normalizing the AHI to < 5 in the majority of patients. For select patients, HNS therapy provides excellent objective improvement in outcome measures.

1. Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by repeated episodes of upper airway narrowing or collapse during sleep often leading to intermittent hypoxemia [1]. Affecting 5–10% of the adult population in the US, untreated moderate to severe OSA has been strongly associated with increased risk of cardiovascular disease and neurocognitive impairment [2–4]. Although continuous positive airway pressure (CPAP) is the primary choice of treatment, suboptimal long-term adherence rates of 40% to 60% have limited its effectiveness [5] [6]. Alternative therapies for these inadequately treated patients with symptomatic OSA have traditionally involved oral appliance therapy as well as a variety of upper airway surgeries including uvulopalatopharyngoplasty (UPPP), genioglossus advancement, hyoid myotomy and suspension, and maxillomandibular advancement [7,8].

Uvulopalatopharyngoplasty (UPPP), usually performed in conjunction with tonsillectomy, corrects obstruction at the level of the

oropharynx with resection of part of the soft palate, uvula, and tonsils, and is the most well established and commonly performed surgical procedure for treatment of OSA. While UPPP reduces the apnea hypopnea index (AHI) and improves symptoms, the procedure has a highly variable success rate, ranging from 30% to 60%. In addition, although it enlarges the upper airway lumen, this traditional surgical approach does not address the inherent increased collapsibility of the upper airway seen in OSA patients [7–9].

Approved by the US Food and Drug Administration in 2014 for treatment of OSA, selective hypoglossal nerve stimulation (HNS) therapy has been shown to reduce upper airway collapsibility and has been proven to be a safe and effective treatment for certain patients with moderate to severe OSA who cannot tolerate CPAP and meet specific inclusion criteria [10–15]. The STAR (Stimulation Treatment for Apnea Reduction) trial demonstrated significant improvements in objective and subjective measures of sleep including AHI and Epworth Sleepiness Scale (ESS) in patients who underwent HNS implantation

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[13]. This study aims to compare outcomes in patients who underwent traditional upper airway surgery, particularly UPPP, to those who underwent HNS therapy for moderate to severe OSA and to evaluate the efficacy of each method in successfully treating OSA.

2. Materials and methods

2.1. Study design and patient selection

This study was designed as a retrospective case series. This research was conducted under Cleveland Clinic Institutional Review Board approved protocol IRB #17-111. Chart review was performed for all patients ($n = 20$) who underwent HNS implantation at a single institution between November 2015 and November 2016. All patients who underwent the procedure were chosen in accordance with selection criteria established by the STAR trial including moderate to severe OSA (AHI between 20 and 65), inability to adhere to CPAP therapy, body mass index (BMI) ≤ 32 kg/m², and absence of complete circumferential oropharyngeal collapse on drug-induced sleep endoscopy (DISE). With 1 of 2 senior authors as lead surgeons for all cases (AHK, DT), the Inspire implantable HNS system (Inspire Medical Systems, Minneapolis, Minnesota, USA) was implanted in each patient using previously published surgical techniques [16]. Patients were discharged home the same day. Device activation and initiation of therapy was completed at 1 month after surgery with follow up polysomnography testing done 2–3 months after implantation.

In addition, a pre-existing database of patients ($n = 116$) who were intolerant of CPAP and underwent UPPP by senior author, AHK, between 2003 and 2012 was accessed. From this data, patients who matched the inclusion criteria used for HNS therapy including AHI between 20 and 65 and body mass index (BMI) ≤ 32 kg/m² were selected ($n = 20$). Of note, these patients did not undergo drug induced sleep endoscopy pre operatively; in office physical examination of the upper airway using direct visualization and flexible laryngoscopy, Friedman tongue position, Mallampati classification, and Muller's maneuver were used for pre operative evaluation and to determine the level of obstruction in these patients. All patients underwent UPPP using the uvulopalatal flap technique or the expansion sphincter pharyngoplasty technique. Tonsillectomy was always performed if tonsils were still present. Some patients also underwent additional procedures including adenoidectomy, septoplasty, and inferior turbinate reduction simultaneously. All patients were admitted overnight for observation. Patients were evaluated in outpatient clinic 4 weeks after surgery. The timing of follow up polysomnography ranged from 2 to 13 months after surgery with most patients (17/20) completing the postoperative sleep study between 3 and 6 months. Of note, there were several patients in both the UPPP and the HNS group who had undergone previous upper airway surgery and presented with persistent signs and symptoms of OSA.

2.2. Data collection and statistical analysis

Data including age, sex, BMI, history of OSA treatment, pre- and post-operative AHI, self reported pre- and post-operative ESS were obtained for both HNS and UPPP groups. Statistical analyses were conducted using SAS version 13.1 (SAS Institute, Cary, North Carolina, USA). Data are shown as mean \pm standard deviation and/or median and percentiles. Two tailed t -tests were used to compare pre operative and post operative values. p -Values ≤ 0.05 were considered statistically significant. Success criteria (50% or more reduction in AHI and an overall AHI of < 20) were used to define success of surgical therapy in treating moderate to severe OSA [17].

3. Results

Twenty patients underwent HNS implantation between November

Table 1

Comparison of baseline characteristics between uvulopalatopharyngoplasty (UPPP) and hypoglossal nerve stimulation (HNS) patient groups.

Characteristic	UPPP group	HNS group
n	20	20
Age at time of surgery	42.1 \pm 12.2	62.4 \pm 8.9
Gender (male, %)	17/20, 85%	13/20, 65%
BMI (kg/m ²)	27.5 \pm 2.7	28.0 \pm 2.1
Pre-operative AHI	40.3 \pm 12.4	38.9 \pm 12.5
Pre-operative ESS	10.9 \pm 4.9	13.2 \pm 5.5
History of prior upper airway surgery for OSA	50%	35%

Values presented as mean \pm SD, BMI = body mass index, AHI = apnea hypopnea index, ESS = Epworth Sleepiness Scale, OSA = obstructive sleep apnea.

2015 and November 2016. Of the 20 patients, 65% (13/20) were male and 35% (7/13) were female. Mean age was 62.4 \pm 8.9 years. Mean BMI was 28.0 \pm 2.1 kg/m² (Table 1). Thirty five percent (7/20) of patients had undergone previous upper airway surgery for OSA including UPPP (3/20), septoplasty and inferior turbinate reduction (3/20) and mandibular advancement (1/20). Mean pre operative AHI was 38.9 \pm 12.5 (Table 2, Fig. 1). Mean pre operative ESS ($n = 15$) was 13 \pm 4.7 (Fig. 2). Post operative polysomnography was completed on average 72.3 \pm 17.3 days (range 56–133 days) after HNS implantation.

Mean BMI did not change significantly from pre operative to post operative (28.0 \pm 2.1 kg/m² to 28.0 \pm 2.4 kg/m², $p > 0.05$) follow up. Mean AHI decreased significantly from 38.9 \pm 12.5 pre implant to 4.5 \pm 4.8, $p < 0.001$, post implant (Table 2, Fig. 1). All 20 patients achieved an AHI < 20 post implant and all were considered successful responders to therapy in accordance with previously published criteria of surgical success with 50% or more reduction in AHI and an overall AHI of < 20 . Of the 20 patients, 65% (13/20) achieved post operative AHI ≤ 5 , 85% (17/20) achieved post operative AHI ≤ 10 , and 95% (19/20) achieved post operative AHI ≤ 15 (Fig. 3). Mean ESS decreased from 13 \pm 4.7 pre operatively to 8 \pm 5.0, post operatively, $p < 0.001$ (Fig. 2).

From the 116 patients who underwent UPPP from 2003 to 2012, 20 patients matched the same inclusion criteria as the HNS group ($n = 20$). Of the 20 patients, 85% (17/20) were male and 15% (3/20) were female. Mean age was 42.1 \pm 12.2 years. Mean BMI was 27.5 \pm 2.7 kg/m² (Table 1). Fifty percent (10/20) of patients underwent additional procedures at the time of UPPP or prior to UPPP including septoplasty (1/20), septoplasty with inferior turbinate reduction (6/20), adenoidectomy with inferior turbinate reduction (2/20) and hyoid suspension (1/20). Mean pre operative AHI was 40.3 \pm 12.4 (Table 2, Fig. 1). Mean pre operative ESS ($n = 16$) was 11 \pm 4.9 (Fig. 2). Post operative polysomnography was completed on average 164.2 \pm 85.2 days (range 60–395 days) after upper airway surgery with the majority of patients (17/20) completing the post operative sleep study between 3 and 6 months.

Mean BMI did not change significantly from pre operative to post operative (27.5 \pm 2.7 kg/m² to 28.4 \pm 2.8 kg/m², $p > 0.05$) follow up. Mean AHI decreased significantly from 40.3 \pm 12.4 pre operatively to 28.8 \pm 25.4 post operatively, $p < 0.05$, (Table 2, Fig. 1). Forty percent (8/20) of patients had 50% or more reduction in AHI and an overall AHI of < 20 . Mean ESS decreased from 11 \pm 4.9 pre operatively to 7 \pm 3.4, post operatively, $p = 0.001$ (Fig. 2).

4. Discussion

OSA is a chronic disorder with increasing prevalence in the US. While positive airway pressure remains the first line therapy for management of moderate to severe OSA, its effectiveness is limited in many patients due to poor long-term adherence rates [5,18]. Left untreated, these patients are at significantly increased risk for cardiovascular

Table 2

Pre vs. Post AHI values for UPPP and HNS groups.

Cohort	Pre operative AHI		Post operative AHI		Difference (Diff) = Post AHI – Pre AHI	
	mean \pm SD	median	mean \pm SD	median	Diff	p-value
UPPP (n = 20)	40.3 \pm 12.4	38.7	28.8 \pm 25.4	20.8	-11.5	0.02
HNS (n = 20)	38.9 \pm 12.5	37.1	4.5 \pm 4.8	2.7	-34.4	< 0.001

P values obtained using paired 2 tailed t-test ($p < 0.05$), AHI = apnea-hypopnea index.

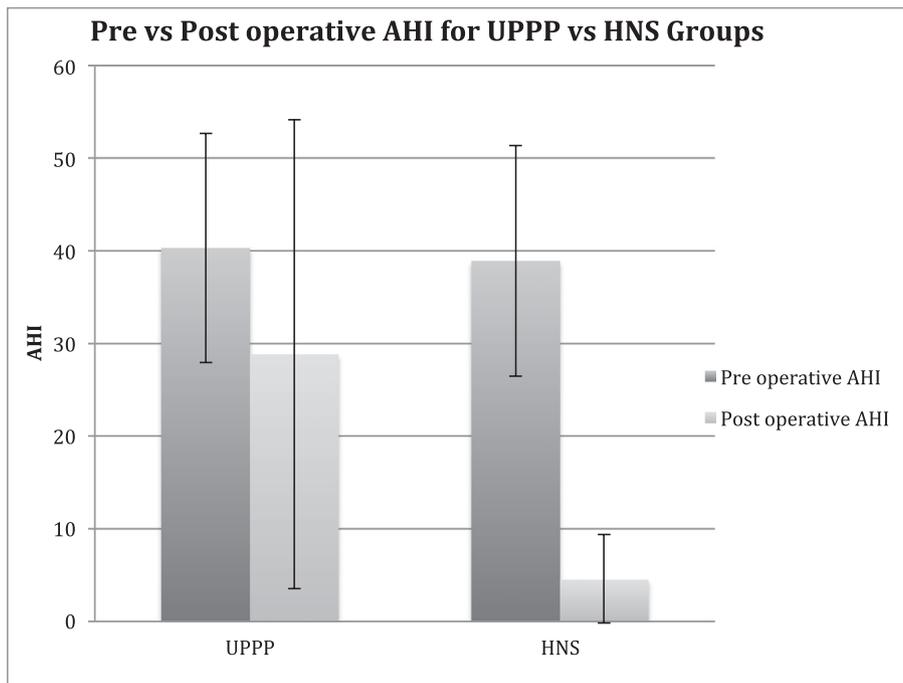


Fig. 1. Pre – and post operative AHI for UPPP and HNS groups. Mean AHI decreased from 40.3 ± 12.4 to 28.8 ± 25.4 , $p < 0.05$, for patients who underwent UPPP. Mean AHI decreased from 38.9 ± 12.5 to 4.5 ± 4.8 , $p < 0.001$, for patients who underwent HNS therapy.

disease and neurocognitive dysfunction. Given the considerable increased morbidity, all-cause mortality, and reduced quality of life associated with moderate to severe OSA, adequate treatment is imperative [2–4,19]. Alternative treatment options for select patients

unable to tolerate CPAP have traditionally included oral appliance therapy, positional therapy, weight loss, and upper airway reconstructive surgery. Currently, surgical treatment options include both conventional upper airway surgery, most commonly UPPP, as well as

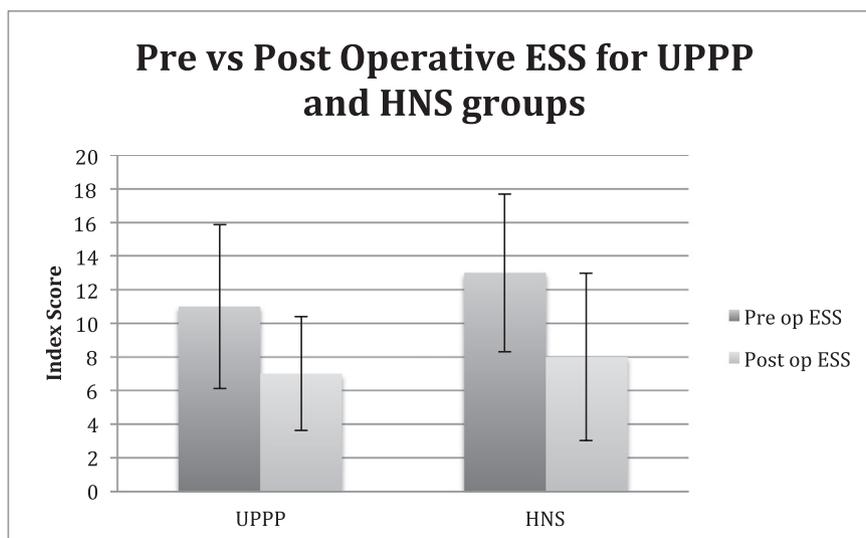


Fig. 2. Pre – and post operative ESS for UPPP and HNS groups. Mean ESS decreased from 11 ± 4.9 to 7 ± 3.4 , $p = 0.001$, for patients who underwent UPPP (n = 16). Mean ESS decreased from 13 ± 4.7 to 8 ± 5.0 , $p < 0.001$, for patients who underwent HNS therapy (n = 15).

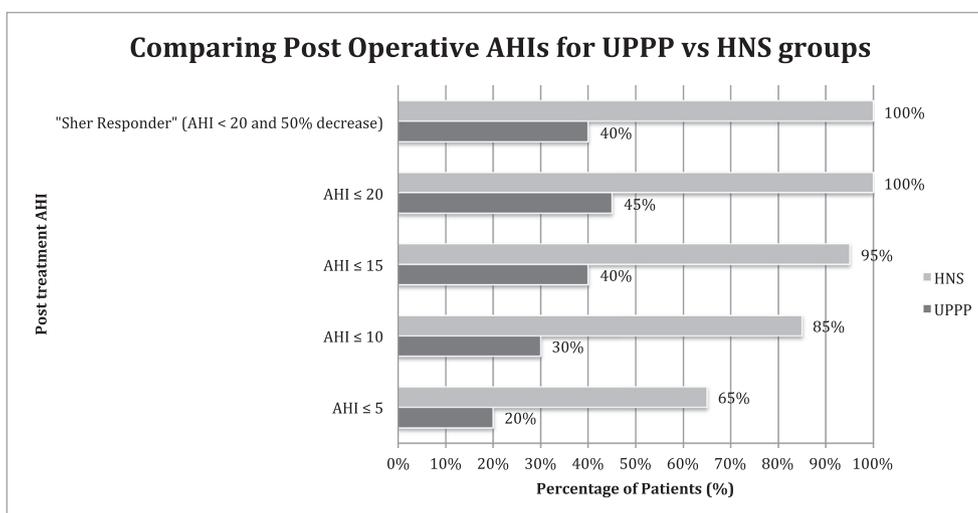


Fig. 3. Comparing postoperative AHIs for UPPP and HNS groups. All 20 (100%) patients in the HNS group achieved a reduction in the AHI of 50% or more and an AHI of < 20 compared to 8/20 (40%) patients in the UPPP group.

HNS, which is now considered second line therapy for select patients with moderate to severe OSA who are not able to adhere to CPAP [8,9,13,20].

To our knowledge, this is the first study to compare outcomes of traditional upper airway surgery, specifically UPPP, the most well established surgical procedure for treatment of OSA, with outcomes of upper airway stimulation therapy (UAS) for treatment of moderate to severe OSA. Baseline characteristics of both cohorts in our data were nearly identical, with the exception of average age, which was significantly higher for the HNS group (Table 1), a difference that can likely be attributed to the insurance approval process for HNS therapy, which is covered by Medicare. In addition, there were patients in both the UPPP and the HNS group who had undergone previous upper airway reconstructive surgery and presented with persistent symptoms of OSA with similar preoperative AHI and ESS as those who had not had any prior treatment. These patients had similar outcomes to those who did not have previous surgery. As shown by Mahmoud et al., prior airway surgery had no statistically significant effect on postoperative AHI [21].

While both UPPP and HNS implantation resulted in significant improvements in the primary objective outcome measure of severity of OSA, the AHI, upper airway stimulation therapy had considerably higher success rate in treating OSA. All patients who underwent HNS implantation were successfully treated in accordance with Sher criteria compared to only 40% of patients in the UPPP cohort. Upper airway stimulation resulted in approximately 90% reduction in AHI while traditional airway surgery resulted in approximately 30% reduction in AHI. In addition, 65% of the patients in the HNS cohort demonstrated a reduction in AHI from the moderate to severe range into the normal range (AHI < 5) compared to only 20% of the patients in the UPPP group. Both surgical treatments resulted in subjective improvements in self-reported sleepiness as calculated by the ESS.

Although our study is limited by small population size along with lack of control groups, the data suggests that the objective improvement in severity of OSA provided by HNS therapy greatly exceeds that seen with UPPP. While long-term data regarding the effectiveness of therapy and any device related side effects is not currently available for our patients in the HNS group, previously published studies have demonstrated the safety and efficacy of HNS. The STAR trial, a large prospective multicenter trial, showed notable reduction in AHI and ESS scores with HNS therapy that remained stable 12, 36, and 48 months after implantation with low rate of long term side effects and device related adverse events [10,12–15]. Kent et al. and Heiser et al. reported

significantly improved objective and subjective outcomes measures with low associated morbidity and excellent voluntary adherence with UAS therapy outside of a clinical trial setting [20,22]. Although studies have shown that UPPP with tonsillectomy is also effective in treating OSA, results have been variable with success rates ranging from 30% when UPPP was performed alone to 60% if it was performed with tonsillectomy. Unlike UAS therapy, which has been proven to offer ongoing and lasting improvement in severity and symptoms of OSA, the efficacy of UPPP in treating OSA has also been shown to decline over time [1,7–9]. In addition, a primary advantage of HNS therapy over UPPP is the ability to address multilevel airway obstruction at both the retroglottal and retropalatal level via palatoglossus coupling, which likely also contributes to the difference in outcomes of the two groups in our study [23].

As HNS therapy is implemented in the routine clinical management of OSA, it is beneficial to know the advantage it offers over alternate surgical treatment modalities. In addition to providing stable, long term improvement in AHI and subjective symptoms in select patients with moderate to severe OSA, HNS therapy is also been associated with decreased hospital stay, reduced pain and need for post-operative opioid medication, and overall lower morbidity compared to traditional pharyngeal and skeletal OSA surgery [10,20]. Our experience suggests that HNS therapy should be offered over UPPP in eligible patients with moderate to severe OSA given the long standing benefits it provides.

5. Conclusion

The present study compares outcomes of the most well established upper airway surgery with outcomes of upper airway stimulation therapy in patients with OSA. Compared to uvulopalatopharyngoplasty, hypoglossal nerve stimulation therapy provides significant objective improvement in outcome measures for select patients with moderate to severe OSA with inability to tolerate CPAP. Although traditional upper airway surgery is effective in treating patients with OSA, our study suggests hypoglossal nerve stimulation is curative for many patients as it normalizes the AHI to < 5 and is an excellent option for second line therapy in select patients with OSA who are intolerant to CPAP.

Disclosures

Dr. Douglas Trask served as a consultant for Inspire Medical Systems. There are no other personal or financial conflicts of interests or disclosures.

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