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Clinical Predictors of OSA Treatment Success Following Implantation of a Hypoglossal Nerve Stimulation Device

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Abstract

Objective. To identify prognostic indicators associated with successful hypoglossal nerve stimulation (HGNS) therapy to treat obstructive sleep apnea (OSA), focusing on patients' physiologic response to awake tongue protrusion.

Study Design. Retrospective chart review.

Setting. Tertiary care center.

Methods. We included consecutive patients with moderate-severe OSA who underwent HGNS implantation from December 2017 to December 2019. Data abstracted include standard demographics, body mass index (BMI), pre- and postoperative apnea-hypopnea index (AHI), and Friedman tongue position (FTP). Additionally, change in hypopharyngeal cross-sectional area on awake tongue protrusion was abstracted. Patients protruded their tongues, and the physician visualized change. Positive change in hypopharyngeal cross-sectional area was documented as +1 and a negative change as −1. Chi-square tests for independence and logistic regression analysis were performed to determine indicators of successful surgery.

Results. Thirty-nine patients were included in this study. Mean ± SD AHI decreased significantly from 43.1 ± 17.36 to 9.18 ± 8.18. Surgical success was achieved in 79.5% of patients. Variables analyzed included BMI >32, preoperative AHI, FTP, and change in hypopharyngeal cross-sectional area on awake tongue protrusion (positive, 65.8%; negative, 34.2%). Positive predictors of success were positive change in hypopharyngeal cross-sectional area (P = .0133), severe OSA (P = .0290), and FTP IIb ($P < .0001$). Negative predictors were BMI >32 (P = .041) and negative change in hypopharyngeal cross-sectional area (P = .02).

Conclusion. Positive change in hypopharyngeal cross-sectional area on awake tongue protrusion and severe baseline AHI were positive predictors of successful HGNS therapy. Negative change in hypopharyngeal cross-sectional area on awake tongue protrusion and BMI >32 were negative predictors.

Keywords

hypoglossal nerve stimulation, upper airway stimulation, obstructive sleep apnea

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Hypoglossal nerve stimulation (HGNS) has emerged as an effective therapy to treat moderate to severe obstructive sleep apnea (OSA) for patients intolerant to continuous positive airway pressure therapy. Current indications for patient selection include body mass index (BMI) ≤32, an apnea-hypopnea index (AHI) of 15 to 65 events/h, and no palatal complete concentric collapse. Despite published criteria, it is evident that the criteria that we use are not accomplishing 100% success. The landmark STAR trial documented 66% of participants achieving treatment success, defined as a 50% decrease in AHI and an AHI <20 events/h.[1] Other published data range from a 68% success rate to 100%.[2,3] This indicates a necessity for studies to identify additional preoperative predictors for successful outcomes.

The physiologic basis of HGNS was identified through animal studies that demonstrated that stimulating the hypoglossal nerve dilated the airway, thereby increasing airflow and decreasing the negative pressure needed to collapse the upper airway.[4] HGNS devices target the branches of cranial nerve XII that innervate the protruder muscles of the tongue. This has proved effective in most patients, although there are some patients who do not respond to the therapy. A study documented a mean negative increase in retroglossal cross-sectional area (CSA) in nonresponders to HGNS surgery.[5] Identifying these patients preoperatively could greatly improve success rates of HGNS surgery.

Up to date, there are few published data focused on the anatomic variations of patients who underwent HGNS surgery. Basic demographics, AHI, and drug-induced sedation endoscopy (DISE) are used as prognostic indicators for HGNS surgery, but persistent suboptimal success rates demonstrate the value of identifying additional factors for patient selection. Studies have shown that hypopharyngeal lumen increases in the majority of patients during voluntary tongue protrusion on awake endoscopy.[6] Some patients,

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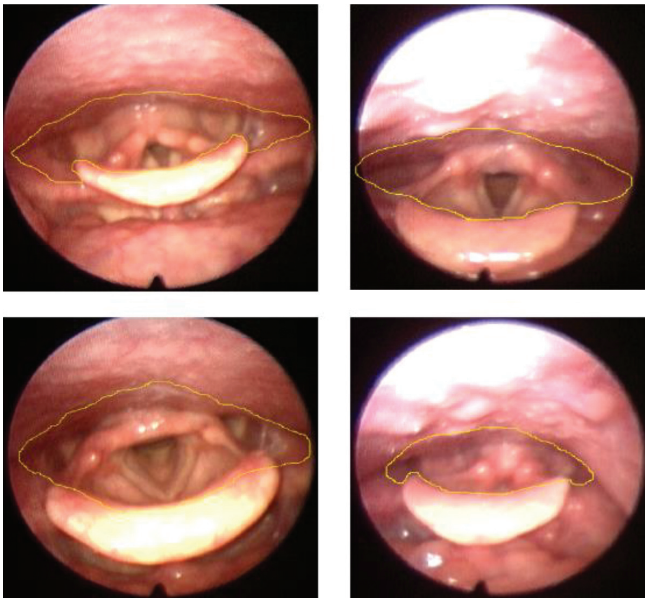

Figure 1. Hypopharyngeal airway response to awake tongue protrusion: typical (left column) vs atypical (right column). Top row: tongue in. Bottom row: tongue out.

though, had a decrease in hypopharyngeal lumen dimensions on tongue protrusion[7] (**Figure 1**). Our hypothesis is that hypopharyngeal airway response on awake tongue protrusion is an accurate indicator of patients' physiologic response to HGNS. Therefore, we may be able to preselect patients for HGNS surgery based on the observed changes in hypopharyngeal CSA on voluntary tongue protrusion.

Methods

Exemption was obtained from the WIRB-Copernicus Group Institutional Review Board. We performed a retrospective cohort study of all patients with OSA confirmed by polysomnography (PSG) who underwent implantation of a HGNS system at a single institution between December 2017 and December 2019.

Based on previously published work by our group,[7] it became evident that the airway response to the mouth-open vs mouth-closed position is not comparable among all patients. Specifically, the mouth-open position usually decreases the area of the hypopharyngeal airway, but in some patients it increases the area. Similarly, tongue protrusion usually increases the area of the hypopharyngeal airway in the awake patient but not always. Based on this work, it became standard to record either a positive response (increased hypopharyngeal airway area) or a negative response (decreased area) in all of our patients with OSA.

Awake nasal endoscopy was performed by a trained otolaryngologist with the patient in a seated upright position during nasal breathing. The endoscope was inserted through the nasal cavity until the hypopharyngeal airway was visualized. Initial visualization was assessed with the patient's mouth open and tongue in neutral position. The patients were then instructed to protrude the tongue. The area assessed included the base of the tongue to the vocal cords to identify increased vs decreased space. Epiglottis collapse or obstruction was considered a negative response. The effect of tongue protrusion was assessed from the least to most extreme with 5 repeated observations. Approximately halfway between the extremes, the best representative of the general direction of airway change was found by the investigator and noted in the patient's chart. If the repeated observations were not consistent, the task was repeated until the observer felt that a positive or negative response was present. In some cases, a negative or unclear response was recorded.

Patient demographics, anatomic measurements, and PSG results were all collected from the electronic medical record. Demographic data included patients' age, sex, and BMI. Anatomic measurements collected were the Friedman tongue position (FTP) and change in CSA on awake tongue protrusion. Measurements were collected by a single observer during the in-office preoperative evaluation. Change in CSA was evaluated by asking the patients to stick out their tongues during awake endoscopy. The physician visualized the change in CSA and documented it as $+1$ or -1, indicating an increase or decrease from baseline, respectively. AHI was collected by PSG prior to and following HGNS implantation. When a full-night postoperative PSG was unavailable, we collected the AHI values from the titration study. Severity of OSA was categorized as none/minimal (AHI, 5 events/h), mild (5-15), moderate (16-30), or severe (>30). The primary outcome was response to surgery, and success was defined per the Sher criteria of at least a 50% improvement in AHI from baseline with a postoperative AHI <20 events/h.

Statistical analysis of demographics and PSG results is presented as mean (95% CI). Anatomic measurements and treatment outcomes were analyzed with a Cochran-Armitage test for trends, χ^2 test for independence, and logistic regression analysis. $P < .05$ was considered statistically significant.

Results

A total of 40 patients with PSG-confirmed OSA underwent implantation with HGNS. One patient was excluded from the study due to incomplete postoperative PSG results. Patient characteristics are summarized in **Table 1**.

Most patients (84.6%) were male, and the mean age at implantation was 52.9 years (95% CI, 50.0-55.8) with ages ranging from 29 to 71. BMI ranged from 20.57 to 35.85, and mean BMI was 29.58 (95% CI, 28.4-30.7). Mean preoperative AHI was 43.1 events/h (95% CI, 37.5-48.6), and mean postoperative AHI was 9.18 events/h (95% CI, 6.5-11.9). AHI values are categorized in **Table 2**. Surgical success defined by the Sher criteria was achieved in 79.5% of patients (n = 31).

Anatomic measurements taken in office at the preoperative evaluation included FTP and change in CSA on awake tongue protrusion. When assessed by FTP, 26 patients (68.4%) had FTP III, 6 had FTP II (15.8%), and 6 had FTP IV (15.8%). The typical response of positive change in CSA on tongue protrusion was visualized in 65.8% of patients, and 34.2% exhibited the atypical response of negative change in CSA (**Table 3**).

Table 1. Patient Characteristics: MEANS Procedure.[a]

Variable	No.	Min	Max	Mean	SD	95% CL for mean Lower	95% CL for mean Upper	Median	Quartile Lower	Quartile Upper
Age, y	40	29.0	73.0	52.9	9.0	50.0	55.8	52.0	49.0	60.0
BMI	40	20.6	39.9	29.6	3.5	28.4	30.7	29.6	27.8	31.6
Preoperative										
AHI	40	17.4	82.2	43.1	17.4	37.5	48.6	40.6	26.4	54.7
O_2 saturation	39	86.0	95.6	92.1	1.9	91.5	92.8	92.3	91.0	93.5
O_2 saturation nadir	40	65.0	89.0	79.3	6.6	77.2	81.4	80.0	73.8	85.0
Postoperative										
AHI	39	0.0	32.6	9.2	8.3	6.5	11.9	6.5	2.1	15.0
O_2 saturation	24	81.7	97.1	92.4	3.1	91.1	93.7	93.0	91.3	94.6
O_2 saturation nadir	24	70.0	94.0	86.8	6.7	84.0	89.6	89.0	83.0	91.5

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; CL, confidence level.
[a]The MEANS procedure on SAS software provides data summarization tools to compute descriptive statistics for variables across all observations and within groups of observations.

Table 2. AHI: Pre- and Postoperative Values (39 Patients).

	Preoperative AHI Mean ± SD	Preoperative AHI No.	Postoperative AHI Mean ± SD	Postoperative AHI No.
Total	43.1 ± 17.36		9.18 ± 8.18	
Severe, >30	51.1 ± 13.8	28	32.6	1
Moderate, 16-30	22.8 ± 3.0	11	20.4 ± 2.54	8
Mild, 6-15		0	8.84 ± 2.92	16
Minimal/none, 0-5		0	1.5 ± 1.15	14

Abbreviation: AHI, apnea-hypopnea index.

Table 3. Change in CSA vs Surgical Outcome.[a]

Change in CSA	Surgical success	Surgical failure
+1	23 (92)	2 (8)
−1	8 (61.5)	5 (38.5)

Abbreviation: CSA, cross-sectional area.
[a]Values are presented as No. (%).

We evaluated surgical success against patient demographics and anatomic variables. Patients with BMI >30 vs ≤30 did not have a higher chance of failure (χ^2 = 0.088, P = .910), but patients with BMI >32 did have a higher chance of failure (χ^2 = 0.396, P = .041). Severe preoperative AHI resulted in a higher frequency of successful outcome (χ^2 = 0.4294, P = .0442); 82% of patients with severe preoperative AHI had successful outcomes. A χ^2 test for independence was run to see if a decrease in airway CSA on awake tongue protrusion and failed outcomes were related. The test results were significant (χ^2 = 3.60, P = .02), indicating that patients who experience a decrease in CSA with tongue protrusion are more likely to have a failed outcome than patients with an increased CSA.

Logistic regression analysis shows that predictors of success include increasing hypopharyngeal CSA on awake tongue protrusion (odds ratio, 3.42; 95% CI, 1.076-1.873; P = .0133), severe AHI (odds ratio, 1.3; 95% CI, 0.0432-0.901; P = .0290), and FTP IIb (odds ratio, 6.905; 95% CI, 3.137-15.202; P < .0001).

Discussion

HGNS has been verified as a reliable alternative for patients with OSA who are intolerant of continuous positive airway pressure. In a feasibility study Van de Heyning et al established many of the baseline parameters for patient selection, which are widely used to determine candidacy for implantation.[8] Vanderveken et al reported that complete concentric collapse of the palate identified during DISE may predict inferior response to HGNS.[9] However, due to imperfect success rates with the current guidelines for patient selection, we looked at some parameters that had previously been established, as well as anatomic characteristics that have not been explored in previous literature—specifically, the effect of awake tongue protrusion on the hypoglossal airway—to identify clinical predictors to improve success rates.

Body Mass Index

Van de Heyning et al[8] identified BMI >32 as a negative predictive factor for success. Thaler et al[10] and Heiser et al[11] noted 8.5% and 9% decreases, respectively, in probability of surgical success per unit increase in BMI among patients in the ADHERE registry. However, other studies have shown that BMI >32 is not a significant predictor of failure.[12] Huntley et al evaluated patients with a BMI >32 (mean, 34.37) who underwent implantation, and they found no difference in postoperative AHI, O_2 desaturation nadir, Epworth Sleepiness Scale score, rate of success, or rate of patients reaching an AHI <15 or <5.[13] We found that a BMI >32 was a statistically significant negative predictor of treatment success vs BMI ≤32.

Baseline AHI

HGNS is recommended for patients with a baseline AHI between 20 and 65 events/h. However, studies have reported mixed results in patients with higher baseline AHI. Evans et al reported that each point increase in baseline AHI decreases postoperative AHI by 1.03, indicating increased surgical success with higher preoperative AHI.[14] Other studies have shown greater benefit with higher baseline AHI,[15] even those >65 events/h.[12] In our study, 82% of patients with severe OSA achieved surgical success, which was significantly associated with treatment success as compared with moderate baseline AHI. Other studies have not found a statistically significant association.[10,11] Thaler et al stated that higher baseline AHI was a negative predictor of success when using other definitions of success, specifically AHI <10 or AHI <10 and 50% decrease in AHI.[10] Nevertheless, the Sher criteria are widely used in the literature to define treatment success.

Friedman Tongue Position

Outside of DISE findings, anatomic variability as a prognostic indicator for HGNS therapy has barely been explored in the literature. Our data revealed that FTP IIb achieved statistical significance as a positive indicator for treatment success as compared with FTP III and FTP IV. However, our limited patient sample with FTP IIb is not enough to make a definitive conclusion that it is a positive predictor for successful HGNS therapy. Additional studies are needed to explore the relationship between FTP IIb and HGNS outcomes.

Of our patients with FTP III, 84.6% achieved surgical success, as opposed to only 50% with FTP IV. Xio et al reported that the rate of surgical success in patients with FTP IV was not significantly different from FTP II and FTP III, yet patients with FTP IV were significantly less likely to achieve surgical cure (AHI <5).[16] Although the values of FTP III/IV did not achieve statistical significance in our study, this may be a result of inadequate sample size, and additional studies may be needed to properly assess the relationship with HGNS outcomes.

Change in CSA on Awake Tongue Protrusion

Stimulating the protruder branches of the hypoglossal nerve causes an increase in hypopharyngeal CSA in most people. Studies have shown that selective stimulation of the protruder branches is associated with good clinical outcomes.[1,10] Oliven et al stated that coactivation of the protruder and retractor muscles of the tongue improves airway patency and increases airway CSA, although it does not have any advantage over genioglossus stimulation alone.[17] Therefore, we hypothesized that although voluntary tongue protrusion involves protrusion and elevation of the tongue, the effect of awake tongue protrusion on the hypopharyngeal airway is a reliable indicator of the effect that asleep HGNS has on the airway. Friedman et al reported that 38% of the patients in the study had a decrease in CSA with awake tongue protrusion, with no difference in patients with or without OSA.[7] Goding et al noted a decrease in retropalatal CSA during asleep hypoglossal stimulation in 35% of the patients in the study.[18] Mann et al recorded a decrease in anterior-posterior diameter during awake genioglossus stimulation in 21.4% of patients, although they attributed this finding to possible electrode displacement.[19] We found a similar pattern among the patients in our study. Of our patients, 34.2% (13/38) exhibited decreased CSA on tongue protrusion, and 38.5% (5/13) of those had a failed outcome, as opposed to 8% (2/25) with increased CSA. Negative change in CSA was significantly associated with treatment failure, and positive change in CSA was significantly associated with treatment success. To date, no literature has examined this variable for patient selection. This measurement is easily obtainable with flexible nasal endoscopy and could have predictive value for treatment success.

HGNS is a relatively new treatment for OSA, and current guidelines for patient selection are inadequate. Our data indicate that there are easily obtainable variables that may aid in patient selection. Further studies are warranted to evaluate the predictive value of change in CSA on awake tongue protrusion and FTP.

Conclusion

HGNS therapy shows significant improvement in OSA outcomes. In a single institution, increase in CSA on awake tongue protrusion and severe baseline AHI were positive predictors of treatment. BMI >32 and decreases CSA on awake tongue protrusion were negative predictors of treatment success. However, due to the limitations outlined previously, our conclusions are best utilized as a pilot study. Further investigation is needed to define these patient characteristics as prognostic indicators for HGNS.

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Author Contributions

Avrahan Boroosan, study conception and design, data collection and interpretation, manuscript writing and editing; **Anna M. Salapatas**, statistical analysis, manuscript editing; **Michael Friedman**, study conception and design, data interpretation, manuscript editing.

Disclosures

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