Read all three of our prestigious publications, each offering high-quality content to keep you informed with the latest developments in the field.

**Laryngoscope**

**The Laryngoscope**

Founded in 1896

Editor-in-Chief: Samuel H. Selesnick, MD, FACS

The leading source for information in head and neck disorders.

[Laryngoscope.com](http://Laryngoscope.com)

**Investigative Otolaryngology**

**Investigative Otolaryngology**

Editor-in-Chief: D. Bradley Welling, MD, PhD, FACS

Rapid dissemination of the science and practice of otolaryngology-head and neck surgery.

[InvestigativeOto.com](http://InvestigativeOto.com)

**ENTtoday**

**ENTtoday**

A publication of the Triological Society

Editor-in-Chief: Alexander Chiu, MD

Must-have timely information that Otolaryngologist-head and neck surgeons can use in daily practice.

[Enttoday.org](http://Enttoday.org)

**WILEY**
INTRODUCTION

Obstructive sleep apnea (OSA) is a disorder occurring during sleep that results from repetitive partial or complete collapse of the upper airway. Effective surgical treatment of OSA is based upon stabilization of the collapsible segments of the airway creating a patent airway for respiration during sleep. Numerous surgical techniques have been developed in an attempt to remedy these areas of collapse. Presently, no surgical modality other than maxillomandibular advancement (MMA) provides a ubiquitously consistent reduction in apnea-hypopnea index (AHI) in all patients.1 This failure places the burden to achieve successful surgical treatment squarely on appropriate patient selection.

Drug-induced sleep endoscopy (DISE) is utilized to evaluate airway collapsibility and to identify suitable surgical procedures for patients with OSA.2–6 DISE is generally performed with propofol, midazolam, or dexmedetomidine and appears to approximate stage 2 sleep.7 The predictive value of DISE has recently come into question by Pang et al.,8 demonstrating no difference in postoperative AHI between patient groups that did and did not undergo DISE prior to surgery. This is contrary to numerous studies that have established DISE as a valuable tool.5–6 Regardless, the Food and Drug Administration now requires DISE to be performed on all patients undergoing evaluation for hypoglossal nerve stimulation (HGNS).

In the last decade, HGNS has become an effective treatment of OSA in select patients. HGNS is an implantable device, similar to a pacemaker, that selectively stimulates the tongue protrusion branches of the hypoglossal nerve during sleep in timing with the patient’s respiration. DISE findings have been shown to predict failed and successful treatment outcomes with HGNS therapy.9,10

The identified concepts of anterior–posterior palatal collapse and complete concentric collapse (CCC) at the level of the soft palate have yielded discriminating predictors for successful HGNS therapy based on DISE.
examination. In 2017, Heiser et al. performed awake endoscopy, DISE, and oral tongue motion examination with and without stimulation on 20 male patients having undergone HGNS implantation. They found that patients having greater contribution from the oral pharyngeal lateral walls during pre-HGNS DISE had smaller enlargement of the retropalatal space on DISE with HGNS stimulation. In addition, both clinical experience and previous data suggest that responders of HGNS exhibit greater opening in the retropalatal dimension than nonresponders.

Mandibular advancement devices (MAD) represent a leading nonsurgical alternative to positive airway pressure (PAP) therapy. Both therapeutic PAP level and airway opening response to mandibular advancement (MA) on DISE have been shown to predict successful treatment of OSA with a MAD. Recently, our group has shown that akin to MAD patients, HGNS patients with low therapeutic PAP levels are more likely to succeed compared to patients with higher pressure requirements. At present, it is unclear if response to MA during DISE can similarly aid in the selection of HGNS candidates. Here we sought to answer the following research question: What is the value of mandibular advancement simulation during DISE in predicting success for HGNS, namely the response at the soft palate and lateral walls to MA? Our primary aim was to test the association between the effect of MA on the velum and lateral walls during MA would achieve greater AHI improvement. Our secondary aims included testing the association with AHI on the response of opening at individual subsites with MA and obstruction at combined and individual subsites before MA.

MATERIALS AND METHODS
All subjects were drawn from the senior author’s clinical practice (R.C.D.) at the Emory Sleep Surgery Center, Emory Midtown Hospital (Atlanta, GA) from October 2015 to January 2019. Institutional review board (IRB) approval was obtained through the Emory University IRB (IRB00088402).

The inclusion criteria consisted of patients who were: 1) English speaking; 2) age ≥22 years; 3) body mass index (BMI) ≤35 kg/m²; 4) AHI ≥15 on most recent diagnostic sleep study (type I or III including WatchPAT [Itamar Medical, Caesarea, Israel]); 5) central or mixed respiratory events <25% of total AHI; 6) failure of first line therapy (continuous PAP or MAD); 7) underwent DISE examination prior to HGNS implantation; 8) underwent HGNS implantation surgery; 9) underwent in-lab HGNS titration sleep study; and 10) underwent treatment efficacy sleep study (type I or III including WatchPAT). Exclusion criteria included: 1) lack of MA on DISE examination; 2) having previous cleft palate or major reconstructive surgery within the oral cavity involving free tissue transfer; and 3) insufficient efficacy sleep study data.

Medical record extraction was conducted by a trained research assistant. The data were manually entered in a deidentified manner into an Excel spreadsheet (Microsoft, Redmond, WA). The measures extracted from the electronic medical record at the preoperative visit included age, sex, BMI, and Epworth Sleepiness Scale (ESS).

Routine HGNS Clinical Care
All patient had a diagnostic sleep study (type I or III including WatchPAT) performed prior to consideration for DISE exam and HGNS implantation. The DISE procedure was performed in the endoscopy suite or the operating room with the patient in the supine position on a stretcher or the operating table. Sedation was induced under bispectral index or SedLine (Masimo, Irvine, CA) sedation monitoring by intravenous administration of propofol utilizing microboluses by an experienced anesthesia team to achieve an optimal plane of anesthesia representing clinical sleep. With the patient breathing spontaneously, the procedure was initiated once snoring was observed. Endoscopy was performed with a flexible fiberoptic laryngoscope with visualization on a monitor and recording on a digital recorder. All exams were downloaded and stored on the password-protected institutional network behind a secure firewall.

Mandibular advancement was performed in a standardized fashion for each patient, and overjet and overbite were documented at the start of the procedure. The mandible was advanced to two-thirds of its maximal protrusive range with a 10-mm open bite. The advancement was performed gradually and gently so as to not elicit an arousal from sedation. In cases where an arousal was evident, the MA was relaxed and reapplied once a deeper plane of anesthesia was achieved.

All HGNS implantation surgeries were performed by the senior author (R.C.D.) at a single site (Emory Midtown Hospital). Implantation was performed in accordance with established standardized surgical practices for this device with an Inspire (Golden Valley, MN) technician present for support throughout the case. Patients received follow-up by the senior author (R.C.D.) at predetermined regular intervals, initially at 10 days postoperatively for surgical wound healing assessment and then at 4 to 6 weeks postoperatively for device activation; an in-lab HGNS titration sleep study was scheduled following this visit. A 3-month follow-up was scheduled to assess patient use and comfort with the device, and an efficacy sleep test was scheduled following this visit. There was a final standard follow-up at 6 months postoperatively to review results of the efficacy sleep test.

DISE Scoring
Each DISE recording was reviewed with event timings (e.g., initiation of MA) recorded in a separate document by the first author (G.B.M.) to streamline further review of relevant portions of the examination. The DISE videos were independently scored by the first and senior author (G.B.M. and R.C.D.). Prior to scoring, the two authors performed 10 cases under joint review to identify discrepancies in interpretation of the planned scoring criteria and to achieve consensus for scoring.

Collapse at the level of the soft palate, tongue base, and epiglottis were graded at optimal sedation, as previously described for evaluation of VOTE (velum, oropharynx, tongue base, and epiglottis) criteria, prior to mandibular advancement and again after mandibular advancement was applied. The position of the lateral pharyngeal walls was made at the junction of the uvula and the soft palate to maximize consistency among patients. The degree of velum and lateral wall collapse was made as a comparison before and after application of mandibular advancement by the following grading criteria: 0 = minimal...
(0%–49%), 1 = moderate (50%–89%), 2 = complete/near complete (90%–100%).

Degree of obstruction included static obstruction (e.g., large noncollapsing tongue) and/or dynamic collapse. The epiglottis site was scored as obstructing if epiglottis collapse occurred independent of tongue collapse. Any discrepancies between the two reviewers for the pre- and postmandibular advancement grades scores were adjudicated by mutual review and consensus.

**Outcome Assessment**

The baseline AHI was extracted from preoperative sleep studies. All subjects in this study had a full-night efficacy study available with AHI and oxygen desaturation index for review. Cloud (Inspire) was used, when available, to confirm therapy compliance for home efficacy studies. The change in AHI (dependent variable) was determined as the difference between preoperative and postoperative studies.

**Statistical Analysis**

The distribution of DISE scores related to response to mandibular advancement naturally stratified into groups. Therefore, the difference between groups was calculated with a paired t test for groups of two and analysis of variance for groupings of three or more by the change in AHI. Primary, secondary, and exploratory analyses were similarly performed to identify possible associations with AHI improvement. Specifically, analysis using baseline DISE scoring (without mandibular advancement) was performed for the secondary analysis. All analyses were performed with JMP Pro 13.0.0 (SAS Institute, Cary, NC).

**RESULTS**

Forty-six patients were included in this study. The mean demographic, subjective, and polysomnographic data are represented in Table I. The cohort had a modest male predominance, with overweight to class I obese patients (BMI = 25–35 kg/m²) in their seventh decade on average. The mean ESS was greater than 11, indicating an excessively sleepy patient population,17 and the baseline polysomnographic data suggest a severe sleep apnea patient population.

**Table I.** Baseline Characteristics of Patients (N = 46).

| Variable | Mean ± SD
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>64.4 ± 15.2</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>27 (59)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.5 ± 3.7</td>
</tr>
<tr>
<td>Symptoms and quality of life</td>
<td></td>
</tr>
<tr>
<td>Epworth Sleepiness Scale†</td>
<td>11.1 ± 6.5</td>
</tr>
<tr>
<td>Polysomnogram, events/hr</td>
<td></td>
</tr>
<tr>
<td>Baseline apnea-hypopnea index</td>
<td>39.4 ± 17.0</td>
</tr>
<tr>
<td>Baseline oxygen desaturation index‡</td>
<td>21.1 ± 17.7</td>
</tr>
</tbody>
</table>

†Values are presented as mean ± SD unless otherwise indicated.
‡Score: 0 to 24; worst = 24.

The mean AHI improved from 39.4 (standard deviation [SD] = 17.0) to 21.1 (SD = 17.7) (P < .01). The ESS decreased significantly with HGNS therapy (11.1, SD = 6.5 vs. 7.3 SD = 6.4, P = .003) demonstrating a clinically meaningful reduction (≥ 2 points) in sleepiness.

**Primary Outcome: Change in Velum and Lateral Walls With Mandibular Advancement**

The change in collapse at the level of the soft palate and lateral walls in response to MA are represented in Figure 1. The subjects from the study cohort naturally stratified into two groups, a minimal opening of collapse (n = 36) and a robust opening of the soft palate and lateral wall in response to MA (n = 10). There was a significant difference in response to HGNS therapy between these groups, with the minimal opening group having a

---

Fig. 1. One-way analysis of change in AHI (baseline–efficacy) by response of V and O combined to MA. AHI = apnea-hypopnea index; MA = mandibular advancement; O = lateral walls; V = soft palate.

Laryngoscope 130: December 2020 Mulholland and Dedhia: Mandibular Advancement During DISE 2919
greater mean decrease in AHI of 21.1 (95% confidence interval [CI]: 15.1 to 29.0) compared to 4.9 (95% CI: −8.3 to 18.0) (P = .02).

Secondary Outcomes
In examining change in collapse of individual subsites with MA, only change in collapse for the lateral walls showed significance (Fig. 2). Again, the subjects from the study cohort naturally stratified into two groups. The group of patients with decreased opening of the lateral wall in response to MA (n = 40) demonstrated greater AHI improvement than those with increased opening (>90% collapse to <50% collapse) (n = 6), mean AHI reduction of 21.0 (95% CI: 14.5 to 27.6) versus 0.2 (95% CI: −16.9 to 17.2) (P = .03).

Analysis of baseline subsite obstruction showed significant differences for combined soft palate and lateral wall collapse and lateral wall only collapse (Figs. 3 and 4). Patients who had complete collapse at the velum and lateral walls (n = 11) had poorer response compared to patients who had partial collapse of the soft palate and lateral walls (n = 35), AHI reduction of 5.6 (95% CI: −7.0 to 18.1) versus 22.3 (95% CI: 15.3 to 29.4) (P = .02). Patients with partial collapse of the lateral walls (n = 32) had improved AHI reductions compared to those with complete collapse (n = 14), AHI reduction of 22.4 (95% CI: 14.9 to 29.9) versus 9.0 (95% CI: −2.3 to 20.3) (P = .05).

DISCUSSION
This is the first study to specifically explore the utility of mandibular advancement during DISE for prediction of HGNS therapy response. In contrast to our alternative hypothesis, an inverse relationship between degree of response of the velum and lateral walls with MA and successful HGNS therapy was identified. Concomitantly, worse baseline severity of collapse at the level of the lateral walls correlated with worse HGNS treatment outcomes.

From the outset, we anticipated observing a positive relationship between application of MA during DISE (selecting patients for greater palatoglossal coupling) and thus better response to HGNS therapy. Our results indicated the opposite, with patients who were observed to have the most robust opening of their airway with MA having on average a worse response to HGNS therapy. In reviewing the results from our secondary outcome analysis, a possible explanation is that contribution of the lateral walls to collapse of the retropalatal airway is an important consideration. It is important to note that patients who had the most robust response to MA started with complete collapse at both the velum and lateral walls. From our individual subsite analysis, we identified that patients having complete lateral wall collapse prior to MA had significantly worse outcomes with HGNS therapy (Fig. 4). Furthermore, when we looked at the airway subsite predominantly contributing to the collapse, we found that patients had poorer HGNS outcomes when the lateral walls contributed to a greater extent than the velum. We observed no significant correlations for other subsites independently or in combination for prediction of HGNS success. In this way, the minimal-opening group appears to have represented patients with the most compromised upper pharyngeal airway at baseline.

Anatomical predictors of response to HGNS have been identified in a study published by Schwab et al. A group of 13 patients (seven responders and six nonresponders to HGNS therapy) matched for age, BMI, and baseline AHI underwent computed tomography imaging during wakefulness with and without HGNS. Their findings identified patients responding to HGNS therapy had smaller soft palate volume 8,789.33 mm³ (SD = 1,811.37 mm³) for responders compared to 11,394.33 (SD = 2,217.07) (P = .032). Volumetric measurement of the lateral pharyngeal walls was not obtained; however, there was no significant difference in retropalatal volume with stimulation between responders and nonresponders.

DISCUSSION
This is the first study to specifically explore the utility of mandibular advancement during DISE for prediction of HGNS therapy response. In contrast to our alternative hypothesis, an inverse relationship between degree of response of the velum and lateral walls with MA and successful HGNS therapy was identified. Concomitantly, worse baseline severity of collapse at the level of the lateral walls correlated with worse HGNS treatment outcomes.
HGNS during awake endoscopy and DISE. They demonstrated that patients who had a greater increase in retropalatal cross-sectional area with HGNS during DISE where more likely to have improved treatment outcomes with HGNS compared to patients having smaller increases in cross-sectional area.

The lateral wall is a known predictor of OSA severity. Magnetic resonance imaging studies have identified lateral pharyngeal wall collapse in the retropalatal air-space as a predictor of severity of OSA.\(^{19,20}\) Until recently, the primary focus of surgeons has been the retropalatal and retrolingual spaces. Liu et al.\(^{21}\) performed pre- and postoperative DISE on a severe-OSA patient cohort undergoing MMA. They observed significant improvement of lateral wall tension overcoming CCC-driven collapse. MMA thus far is the only surgical procedure that has been documented to predictably treat profound lateral wall collapse effectively.

In the present article we recognize a very significant correlation of obstruction driven by lateral wall collapse and worse HGNS outcomes. We chose a specific anatomic location to observe lateral wall collapse (the break point between where the uvula attaches to the soft palate). This definition may or may not be analogous to the traditional definition of CCC, where CCC is more broadly defined to occur at the level of the soft palate. Since the inception of patient selection criteria for HGNS, patients with CCC have been excluded.\(^{22}\) The findings from our article may add strength to this recommendation for excluding these patients, even though the definition for lateral wall collapse we utilized and the definition for CCC are not synonymous.

There are several limitations in this study. With 46 patients, we have limited power to detect modest differences between groups. However, statistically significant relationships were observed in the present study for the primary and secondary outcomes (contribution of lateral wall collapse). Despite our prospective cohort, the preoperative diagnostic sleep testing types were not standardized due to varied referral sources and insurance carriers. However, a major strength of this study is our use of full-night efficacy studies, as suggested by a recent editorial reporting of HGNS outcomes.\(^{23}\) The DISE procedures occurred for several minutes with different anesthesia providers, making it difficult to standardize execution. There is additional limitation by the fact that DISE videos were reviewed retrospectively, and our group made several decisions related to scoring of DISE videos, such as classification scoring of degree of obstruction and the location at which to evaluate lateral wall obstruction (level of the uvula). These decisions were made from the clinical perspective and for consistency of identification among patients.

**CONCLUSION**

This study illustrates that a robust response to MA on DISE for the soft palate and lateral walls (i.e., upper pharynx) correlates with worse outcomes for HGNS therapy. Furthermore, this study suggests the strong effect of baseline lateral wall obstruction on the efficacy of HGNS treatment. Additional prospective investigation into DISE findings, specifically lateral wall obstruction, should further elucidate optimal candidacy criteria for HGNS patients.

**ACKNOWLEDGEMENTS**

The authors acknowledge Everett G. Seay, RPSGT, who served as the primary research coordinator in this study.

**BIBLIOGRAPHY**