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Association between body mass index and unilateral hypoglossal nerve stimulation efficacy depends on the pattern of pharyngeal collapse in obstructive sleep apnea

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Statistical analysis: DV, SAS, TC

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Drafting the article: DV, SAS, PH

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Sleep Apnea, Obstructive; Drug-induced Sleep Endoscopy; Site of pharyngeal collapse

INTRODUCTION

Unilateral hypoglossal nerve stimulation (HGNS) is an effective alternative treatment for obstructive sleep apnea (OSA) in patients intolerant of positive airway pressure therapy¹, but its efficacy is variable². Elevated body mass index (BMI)³ and pharyngeal collapse patterns with a severe lateral component, including concentric complete collapse at the palate (CCC) and complete oropharyngeal lateral wall (OLW) collapse are both associated with poor HGNS outcomes^{4,5}. Increased BMI worsens upper airway collapsibility⁶, while severe lateral collapse may limit HGNS efficacy because stimulation primarily produces anteroposterior (AP) airway opening. The extent to which BMI and collapse pattern jointly influence HGNS efficacy remains unknown. Clarifying this interaction is clinically important, particularly given recent relaxation of BMI-related FDA eligibility criteria. We therefore examined how BMI modifies HGNS efficacy across collapse patterns, hypothesizing that greater BMI would preferentially worsen outcomes in collapse patterns that are less responsive to HGNS (CCC and complete OLW collapse), but not in predominantly AP collapse. Some of the results of these studies have been previously reported in the form of an abstract⁷.

METHODS

We pooled data from a multicenter retrospective cohort⁴ and a prospective single-center cohort (n=760) with available demographics, DISE-based collapse classification, and baseline and post-treatment sleep studies (approximately 4–6 months post-implantation); both cohorts were from U.S. academic centers, with adults implanted between 2014–2019 in the multicenter cohort (DISE re-scored post hoc by blinded reviewers) and between October 2019 and June 2024 in the prospective cohort (clinical DISE scoring).

All patients underwent DISE according to routine clinical protocols at each institution^{4,5,8} with collapse classified using the VOTE system⁹. Collapse patterns were grouped as lateral (CCC or complete OLW collapse) or AP (complete tongue base, AP velum, or epiglottic collapse). CCC was identified on DISE re-scoring. Patients with complete tongue base collapse were always classified as AP; those with CCC or complete OLW collapse without

complete tongue base were classified as lateral, resulting in mutually exclusive groups. Patients with partial collapse only (n=60) were not included in primary analysis.

HGNS efficacy was assessed as percent reduction in AHI from baseline. Treatment success was defined as $\geq 50\%$ AHI reduction to < 15 events/h.

Multivariable regression evaluated the association between HGNS efficacy and BMI, lateral collapse, and their interaction ($\text{BMI} \times \text{lateral collapse}$), adjusting for baseline AHI, center, follow-up sleep study type, and prior/concomitant pharyngeal surgery. Secondary analyses assessed absolute AHI reduction and treatment success using linear and logistic regression, respectively.

RESULTS

Baseline demographics and AHI were similar between cohorts, supporting pooled analysis. Patients with lateral collapse (n=60, 14 with CCC) were somewhat younger (median: 56 vs. 61 years), more commonly male (86% vs. 71%), with slightly higher BMI (30.1 vs. 28.8 kg/m^2) and AHI (35.9 vs. 31.0 events/h) than patients with AP collapse. Overall, median [IQR] BMI was 29.0 [26.6, 31.3] kg/m^2 , with 117 patients (28%) having BMI $> 32 \text{ kg/m}^2$ and 12 (3%) having BMI $> 35 \text{ kg/m}^2$. Table 1 shows HGNS efficacy and treatment response stratified by collapse pattern and BMI.

For HGNS efficacy (percent reduction in AHI), there was a significant interaction between BMI and lateral collapse ($p_{\text{interaction}} = 0.027$), such that increased BMI was associated with a substantially greater loss of efficacy in patients with lateral collapse ($-19.7 [95\% \text{CI: } -33.0, -6.2]\%$ per 5 kg/m^2) than in patients with AP collapse ($-3.8 [-8.0, 0.36]\%$ per 5 kg/m^2 ; Figure 1). A similar interaction was observed when efficacy was assessed using absolute reduction in AHI ($-5.2 [-10.2, -0.17]$ events/h), with greater BMI-related loss of efficacy in lateral collapse ($-6.4 [-11.1, -1.6]$ events/h per 5 kg/m^2) than in AP collapse ($-1.2 [-2.7, 0.30]$ events/h per 5 kg/m^2).

For treatment success, the interaction between BMI and lateral collapse was significant (odds ratio [95%CI]: 4.1 [1.2, 14.0]). Each 5 kg/m^2 increase in BMI was associated with an approximately four-fold reduction in the odds of successful HGNS response among patients with lateral collapse (4.4 [1.4, 14.3]), whereas BMI was not associated with treatment success in patients with AP collapse (1.1 [0.75, 1.5], Figure 1). Using alternative treatment success definitions, the $\text{BMI} \times \text{lateral collapse}$ interaction on success remained significant ($p_{\text{interaction}} < 0.05$) when success was defined as a 50% AHI reduction to < 10 events/h and as a 70% AHI reduction. For a 5 kg/m^2 increase in BMI, odds ratios [95%CI] for success in lateral collapse were approximately three- to four-fold lower (3.1 [1.1, 9.1] and 4.5 [1.5, 13.7], respectively), whereas BMI was not associated with either definition of treatment success in patients with AP collapse, with odds ratios close to 1 (1.2 [0.79, 1.9] and 1.4 [0.99, 1.9], respectively).

DISCUSSION

This study identifies a clinically important interaction between BMI and pharyngeal collapse pattern, with increasing BMI reducing HGNS efficacy and success in patients with lateral collapse, but having minimal impact in those with anteroposterior (AP) collapse. These findings suggest that recently relaxed BMI eligibility criteria for HGNS may be more appropriate for patients with AP collapse, while caution may be warranted in patients with lateral collapse.

Although greater BMI is a recognized risk factor for reduced HGNS response³, our findings indicate that this effect is largely based on collapse pattern. A 5 kg/m² increase in BMI was associated with an approximately 20% reduction in HGNS efficacy and four-fold decreased odds of treatment success in patients with lateral collapse, whereas the same BMI increase had little effect in patients with AP collapse. However, since only 12 patients had BMI >35 kg/m², whether these findings extend to patients with more severe obesity remains uncertain.

Importantly, these results also suggest that patients with lateral collapse may still benefit from HGNS when BMI is low, rather than being excluded outright from therapy. For such patients, counseling regarding weight management in conjunction with HGNS may be particularly important, as modest weight gain could substantially reduce treatment efficacy. However, only 17 patients had both lateral collapse and low BMI, and therefore the apparently favorable HGNS outcomes observed in this subgroup should be interpreted cautiously.

Several mechanisms may explain why increasing BMI preferentially impairs HGNS efficacy in patients with lateral collapse. Obesity is associated with increased pharyngeal collapsibility⁶, greater parapharyngeal soft tissue mass¹⁰, and reduced lung volumes¹¹, which together may worsen the severity of lateral collapse. As obesity-related increases in lateral airway collapsibility occur, the ability of HGNS-induced tongue protrusion to influence lateral airway patency may be diminished. In contrast, in patients with AP collapse, this pattern of collapse remains directly targeted by HGNS, such that increasing collapsibility has lesser impact on treatment effectiveness. We highlight one limitation that lateral collapse group was dominated by OLW collapse, with relatively few CCC patients, limiting confidence that these findings extend equally to CCC.

In conclusion, BMI substantially modifies HGNS efficacy with lateral but not AP pharyngeal collapse, supporting a more individualized approach to HGNS therapy.

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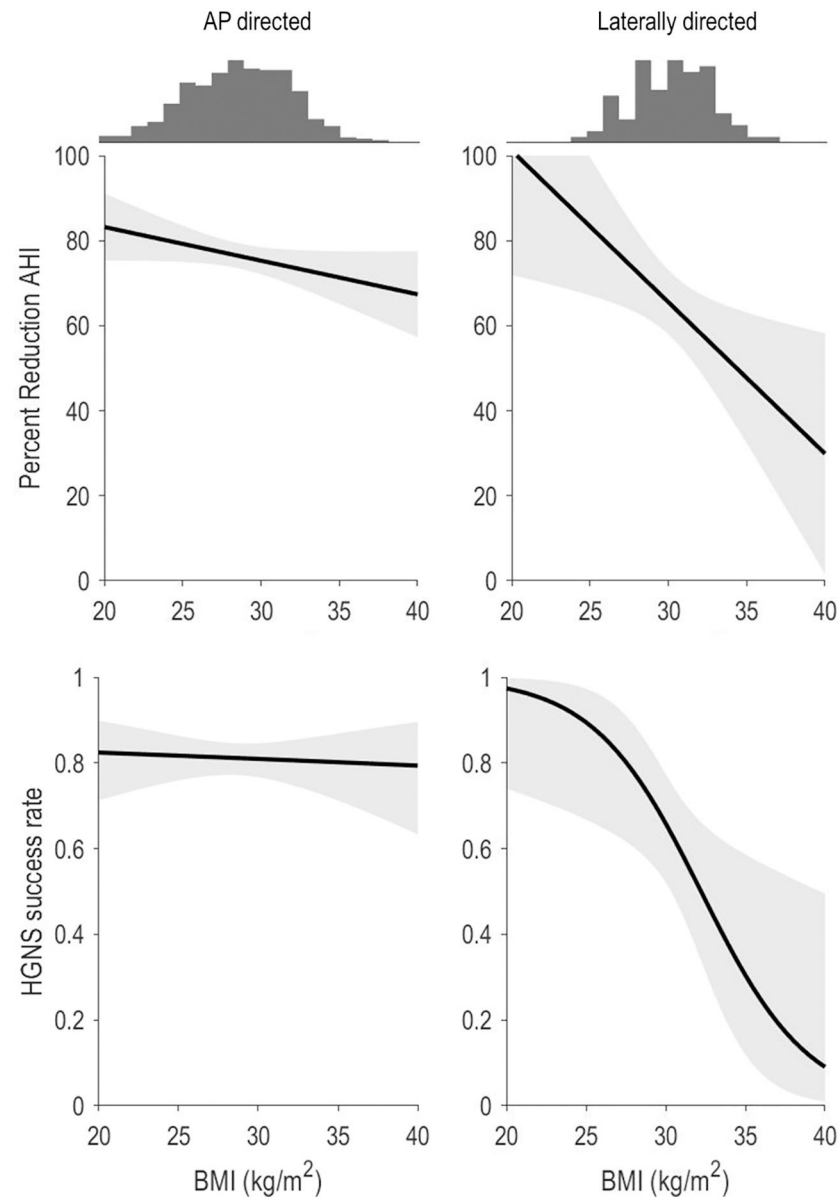


Figure 1. Impact of body mass index (BMI) on hypoglossal nerve stimulation (HGNS) efficacy (percent reduction AHI) and success rate across AP- and laterally directed collapse patterns. Histograms at the top of the figure illustrates the BMI distribution within each pattern of collapse.

Table 1.

Hypoglossal nerve stimulation outcomes in pooled and individual cohorts, stratified by pharyngeal collapse pattern (AP, lateral, and partial) and BMI category (high vs low).

Cohort	Parameter	All	AP		Lateral	
			High BMI (>29 kg/m ²)	Low BMI (≤29 kg/m ²)	High BMI (>29 kg/m ²)	Low BMI (≤29 kg/m ²)
Pooled cohorts	N	712	225	257	43	17
	Percent reduction AHI	84.7 [62.6, 94.8]	82.8 [61.6, 94.0]	87.4 [69.5, 96.4]	63.5 [42.2, 86.6]	85.2 [51.1, 89.4]
	N Success(%)	547 (76.8%)	173 (76.9%)	204 (79.4%)	22 (51.2%)	12 (70.6%)
Multi-center retrospective cohort	N	341	110	101	28	12
	Percent reduction AHI	80.9 [55.5, 92.6]	78.0 [57.2, 91.2]	85.9 [58.0, 96.4]	64.2 [45.5, 88.4]	76.7 [40.1, 90.9]
	N Success(%)	244 (71.6%)	81 (73.6%)	72 (71.3%)	15 (53.6%)	8 (66.7%)
Prospective single-center cohort	N	371	115	156	15	5
	Percent reduction AHI	87.4 [70.5, 96.0]	85.1 [70.6, 95.9]	88.7 [74.0, 96.4]	53.2 [42.2, 84.0]	85.2 [80.5, 89.3]
	N Success(%)	303 (81.7%)	92 (80.0%)	132 (84.6%)	7 (46.7%)	4 (80.0%)

AHI: apnea-hypopnea index; BMI: body-mass index; AP: anteroposterior

AP and Lateral represent the patients categorized as having AP-directed collapse and laterally-directed collapse, respectively.

AP and lateral group counts do not add to the total because patients with only partial collapse (N=60) were classified separately and are not included in either group.

The threshold separating high from low BMI is the median BMI of 29.0 kg/m²

Sample analyzed for this table only includes patients that underwent HGNS-only (n=712), i.e., excludes patients who underwent upper airway surgery (functional expansion pharyngoplasty, tonsillectomy, or partial uvullectomy) concomitant with or prior to HGNS without repeat DISE.