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Characteristic Pressure Waveforms Can Distinguish Airway Collapse Patterns in Sleep Apnea Patients: A Pilot Study

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Abstract

Objective. To use pharyngeal pressure recordings to distinguish different upper airway collapse patterns in obstructive sleep apnea (OSA) patients, and to assess whether these pressure recordings correlate with candidacy assessment for hypoglossal nerve stimulator (HGNS) implantation.

Study Design. Prospective case series.

Setting. Single tertiary-quaternary care academic center.

Methods. Subjects with OSA prospectively underwent simultaneous drug-induced sleep endoscopy (DISE) and transnasal pharyngeal pressure recording with a pressure-transducing catheter. Pressure was recorded in the nasopharynx and oropharynx, and endoscopic collapse patterns were classified based on site, extent, and direction of collapse. Pressure recordings were classified categorically by waveform shape as well as numerically by inspiratory and expiratory amplitudes and slopes. Waveform shape, amplitude, and slope were then compared with the endoscopic findings.

Results. Twenty-five subjects with OSA were included. Nasopharyngeal waveform shape was associated with the extent of collapse at the level of the palate ($P = .001$). Oropharyngeal waveform shape was associated with anatomical site of collapse ($P < .001$) and direction of collapse ($P = .019$) below the level of the palate. Pressure amplitudes and slopes were also associated with the extent of collapse at various sites. Waveform shape was also associated with favorable collapse pattern on endoscopy for HGNS implantation ($P = .043$), as well as surgical candidacy for HGNS ($P = .004$).

Conclusion. Characteristic pharyngeal pressure waveforms are associated with different airway collapse patterns. Pharyngeal pressure is a promising adjunct to DISE in the sleep surgery candidacy evaluation.

Keywords

aerodynamics, drug-induced sleep endoscopy, obstructive sleep apnea, pressure, sleep medicine, sleep surgery

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Obstructive sleep apnea (OSA) is a disorder in which the airway repeatedly obstructs during sleep, leading to oxygen desaturation and sympathetic activation.[1,2] OSA is common in adults, with historical studies observing a 2% to 4% prevalence and more recent systematic reviews showing an even higher prevalence ranging from 9% to 38%.[2,3] Left untreated, OSA results in daytime fatigue and impaired concentration, and it is associated with major cardiopulmonary consequences such as hypertension, heart failure, and stroke.[4-8]

Treatment of OSA can include behavioral modifications, such as weight loss or positional therapy; nonsurgical therapy, such as continuous positive airway pressure (CPAP) or mandibular advancement device; and surgery.[1] CPAP is first-line treatment for moderate to severe OSA. Unfortunately, with the rising prevalence of obesity, as well as CPAP nonadherence rates of 34%, patients with OSA are often referred to or seek out otolaryngologists for surgical options.[9-11] However, wide variation in patient anatomy and obstructive patterns, difficulty evaluating these collapse patterns on exam and imaging, and perhaps an equally wide range of upper airway surgical options, have left a legacy of inconsistent surgical outcomes prior to the widespread adoption of drug-induced sleep endoscopy (DISE).[12-14]

Fortunately, DISE has facilitated a more accurate classification of anatomical collapse patterns and has allowed surgeons to improve patient selection for both

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surgical and nonsurgical treatment options.[15-24] Still, there remains a level of subjectivity in DISE interpretation and classification, as well as the variability of recommendations for the same patient between different surgeons.[25,26] A large multi-institutional study of DISE findings and surgical outcomes showed only moderate interrater reliability.[24] Pharyngeal pressure recordings during both natural and drug-induced sleep have been proposed as a potential tool to further objectify sleep apnea collapse patterns, and have been used since as early as 1992.[27] Since their introduction, pharyngeal pressure catheters during sleep and sleep endoscopy have shown promise in identifying presence or absence of collapse as well as determining the anatomic site of collapse.[27-34] Only recently has this tool been leveraged to improve surgical selection and improve patient outcomes, as described by Tvinnereim et al in the case of patients with upper pharyngeal obstruction on pressure recording who underwent plasma radiofrequency ablation (RFA).[35]

The goal of this pilot study is to demonstrate that the utility of pharyngeal pressure measurement during sleep, specifically during DISE, can be further broadened. We hypothesize that pressure waveforms can be categorized into patterns that correspond with specific endoscopically visualized collapse patterns. Furthermore, we hypothesize that pharyngeal pressure waveforms can be used to predict sleep surgical candidacy. This study assesses that hypothesis by comparing pressure waveforms with candidacy for hypoglossal nerve stimulator (HGNS) implantation. HGNS candidacy was chosen because, unlike many other sleep apnea surgeries, all potential HGNS patients must have a preoperative DISE. Additionally, there are well-defined DISE candidacy criteria for HGNS eligibility: HGNS patients' DISE findings must be free of complete concentric collapse at the palate.[14,36,37] While other interventions (eg, palatopharyngoplasty) may be guided by DISE, DISE is not always necessary for these alternatives. For the purposes of this pilot study, we therefore focused on cases where DISE was strictly required (ie, HGNS workup).

Methods

Study Design

The study was performed prospectively at a single tertiary-quaternary care academic center. and approved by the University of Pennsylvania Institutional Review Board (Protocol #827621).

Subjects with moderate to severe OSA who failed CPAP and were potential candidates for HGNS sleep surgery pending DISE were enrolled. Inclusion criteria were as follows: evaluated by a sleep medicine physician and deemed to have failed CPAP (unable to use or achieve consistent benefit after sufficient attempts), age 22 or above, apnea-hypopnea index (AHI) 15 or above, and being considered for HGNS implantation.

Data Collection

Subjects first underwent routine evaluation in the office including history, complete head and neck physical exam, and awake flexible nasopharyngolaryngoscopy (NPL) in a seated position. Next, subjects underwent simultaneous DISE and transnasal pharyngeal pressure measurement using a flexible pediatric bronchoscope and an approximately 1 mm diameter pressure-transducing catheter (Mikro-Cath, Millar Inc; Supplemental S1-S4, available online). Sedation for DISE was achieved with propofol using a probability ramp infusion as previously described.[38,39] On initiation of the propofol infusion, while the patient was still awake, a flexible bronchoscope was inserted into the nasopharynx (NP) via the subject's naris that appeared to be more patent, and an NPL was performed in the supine position. The scope was then withdrawn to the NP, with the palate in view, and the pressure catheter was inserted in the nose and advanced until visualized in the NP. The pressure catheter was typically inserted into the naris opposite the scope unless resistance was met, in which case it was inserted via the same naris as the scope. Once adequate sedation was achieved, the scope and pressure catheter was advanced in order to evaluate the NP, oropharynx (OP), and hypopharynx and larynx (HPL). When visualizing the NP, the pressure transducer (located at the tip of the catheter) was advanced to the retropalatal level; when visualizing the OP, the transducer was advanced to the retroglossal level. In cases with notable hypopharyngeal or laryngeal collapse, when visualizing the HPL, the transducer was advanced to the retroepiglottic level. Each level was evaluated for 1 minute, with pressure measurements recorded at 100 Hz using a data acquisition system (DI-1120 and WinDaq, DATAQ Instruments Inc). Once the airway was evaluated thoroughly, both the endoscope and pressure catheter were removed, sedation was stopped, and the patient emerged from anesthesia. This was performed in the same manner for each of the 25 subjects.

Data Processing

Endoscopic collapse patterns were classified essentially following the VOTE classification, but the "E" (epiglottis) was broadened into the more general category of supraglottic collapse, as both epiglottic and arytenoid collapse were observed.[40] That is, the site of collapse was categorized into palate (V), lateral OP and tonsils (O), base of tongue (T), and supraglottis (E). In keeping with the VOTE system, extent was categorized into no collapse, partial collapse, and complete collapse; and direction was categorized into AP, lateral, and concentric.

Pressure recordings were classified categorically by waveform shape, and numerically by amplitudes and slopes of both inspiratory and expiratory phases.

For Waveform Shape

On visual pattern analysis of the nearly 1500 breaths captured in total among the 25 subjects' DISE recordings, the authors were able to categorize waveform shapes into 8 recurring archetypes, described in Figure 1A-H. The authors named these: gentle, sinusoidal, ramp, cycloid, square, peak-plateau, peak-col-hill, and shark fin.

For Waveform Amplitude and Slope

Amplitude and slope were calculated in MATLAB (The MathWorks Inc). Swallowing during endoscopy produced large pressure spikes, so a novel waveform swallow filter (beyond the scope of this article) was developed in MATLAB to remove these from the calculations.

Pressure waveform shape, amplitude, and slope were then compared with the endoscopic findings.

Statistical Analysis

Statistical analysis was performed in SPSS (IBM Corporation). Demographics and sleep study metrics are listed in Table **1**. Only pressure tracings in the NP and OP were analyzed. HPL collapse was identified in only 2 subjects, so there was insufficient statistical power for HPL tracing analysis. Analysis was performed separately for each tracing site (NP and OP) and collapse site (V, O, T, E), as tabulated in Table **2**. Using Fisher's exact test, the waveform shape was compared with the endoscopic presence of collapse, the extent of collapse, and direction of collapse. Using analysis of variance (ANOVA), pressure metrics (amplitude and slope) were compared with collapse type (presence, extent, direction). ANOVA was also used to compare waveform shape was compared with pressure metrics.

For each of the 8 waveform shapes, in the NP and OP tracing sites, the mode was determined for presence, site, extent, and direction of collapse. Waveform shapes with a mode showing the presence of collapse, located in the palate or base of the tongue (V or T in VOTE classification), complete or incomplete, and in the AP direction were designated as "favorable waveforms," referring to being favorable for HGNS candidacy. Then, in a secondary analysis, HGNS candidacy was tested using Fisher's exact test to compare favorable waveform status versus favorable endoscopic collapse status, and favorable waveform status versus overall HGNS candidacy (favorable collapse and meeting all FDA criteria: CPAP failure, age ≥ 22, AHI of 15-65, BMI < 32).

For each statistical test group, Bonferroni correction was presented, using a group significance level of 0.05. Table **2** summarizes the resulting individual significance levels per comparison. For example, since there were 12 comparisons for waveform shape versus endoscopic collapse pattern using Fisher's exact test, the Bonferroni correction resulted in a significance level of 0.05/12, or 0.004 (rounded to the nearest thousandth). We present the significance based on the uncorrected thresholds, given the nature of this small pilot study assessing variables for future study, and the belief that Bonferroni corrections are not necessarily appropriate for such studies.[41] However, the results that do not meet the Bonferroni-corrected significance levels are called out for the reader's independent interpretation with a dagger (†).

Results

Twenty-five subjects were included.

Table **3** shows the 8 waveform shapes, the mode of collapse pattern, and the designated favorable waveforms. In the NP, gentle, sinusoidal, ramp, peak-plateau, and peak-col-hill waveforms were favorable waveforms. In the OP, ramp and square waves were favorable waveforms.

Categorical analysis of waveform shape versus collapse patterns using Fisher's exact test identified the following significant associations: NP waveform shape was associated with the extent of collapse at the level of the palate ($P = .001$). OP waveform shape was associated with the presence of palate collapse ($P = .042^{\dagger}$), anatomical site of collapse below the palate ($P < .001$), and direction of collapse ($P = .019^{\dagger}$) below the level of the palate. OP waveform shape compared with extent of collapse below the palate trended towards significance ($P = .055^{\dagger}$). When further subdividing oropharyngeal sites, there were several more significant associations. For lateral oropharyngeal wall/tonsil collapse, OP waveform shape was significantly associated with the presence of lateral oropharyngeal wall/tonsil collapse ($P = .011^{\dagger}$), extent of collapse ($P = .022^{\dagger}$), and direction of collapse ($P = .011^{\dagger}$). For base of tongue collapse, OP waveform shape was significantly associated with the presence of base of tongue collapse ($P = .005^{\dagger}$) and extent of collapse ($P = .037^{\dagger}$). For supraglottic collapse, OP waveform shape was significantly associated with the presence of supraglottic collapse ($P < .001$), extent of collapse ($P < .001$), and direction of collapse ($P < .001$).

ANOVA analysis of pressure metrics versus collapse type showed that no collapse, incomplete collapse, and complete collapse could be distinguished by pressure amplitude and slope. For NP measurements, pressure amplitude versus presence of collapse at the palate was statistically significant ($P = .002$), with amplitude being lower in cases of no collapse. When compared to extent of collapse at the palate, pressure amplitude and slope were both significant ($P < .001$ and $P = .014^{\dagger}$, respectively), with the lowest values associated with no collapse, intermediate values with incomplete collapse, and highest pressure amplitudes and slopes associated with complete collapse. For OP measurements, pressure slope was significantly associated with extent of collapse below the level of the palate ($P = .018^{\dagger}$), again with complete collapse having the highest slope.

ANOVA analysis of waveform shape versus pressure metrics identified the following significant associations:

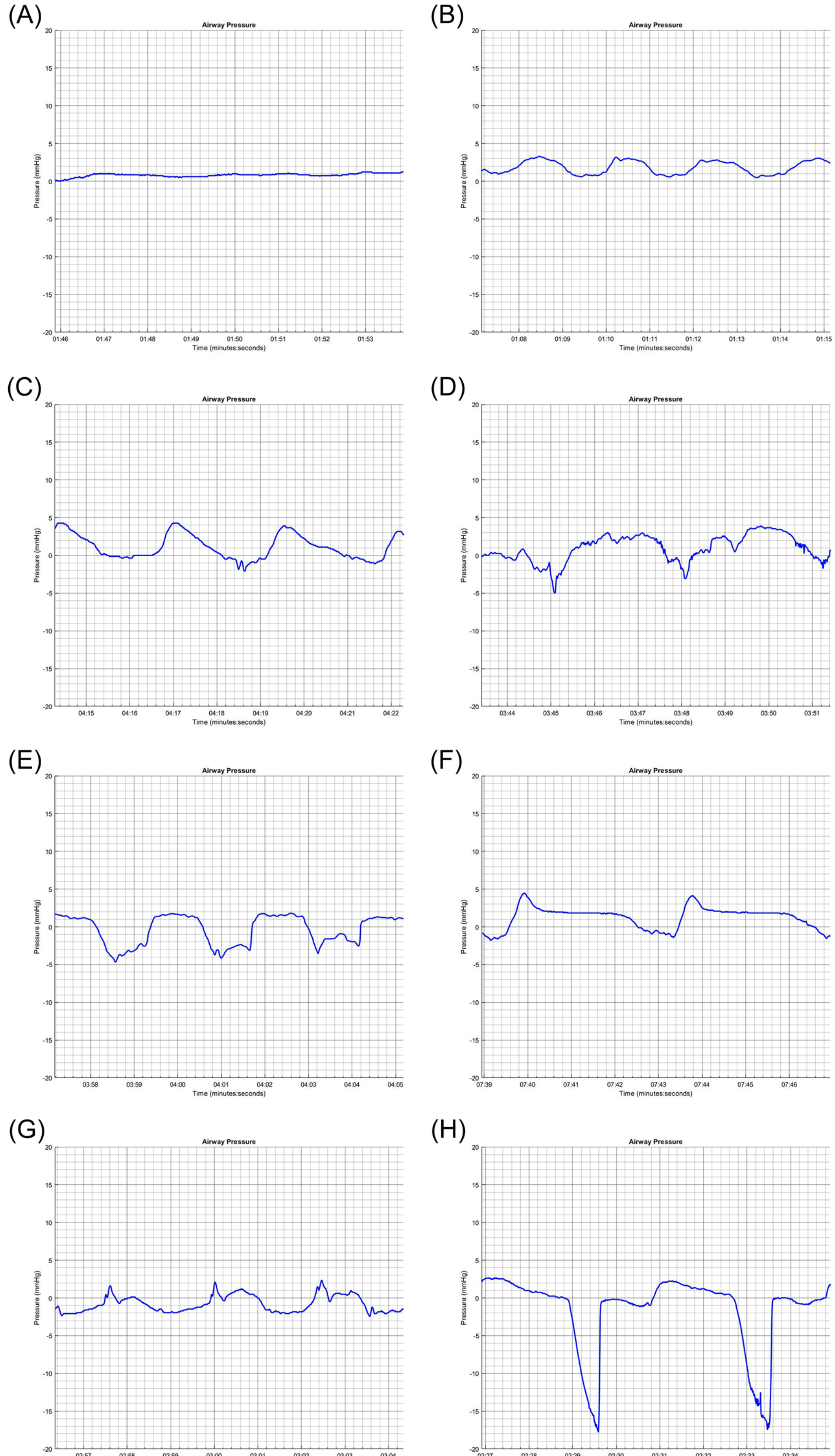

Figure 1. Characteristic waveform shapes on pharyngeal pressure tracings. (A) "Gentle," characterized by flat or minimal peaks and troughs; (B) "Sinusoidal," smoothly rolling peaks and troughs akin to a sine wave; (C) "Ramp," sharp rise followed by a sloping descent; (D) "Cycloid," semicircular peaks with sharply transitioning troughs; (E) "Square," sharp transitions between peaks and troughs with relative plateaus at each; (F) "Peak-Plateau," sharp rise to a peak with a partial descent, plateau, and then sloping descent back to baseline; (G) "Peak-Col-Hill," similar to peak-plateau but with a second smaller, rounded hill in place of the plateau; and (H) "Shark Fin," moderately rounded peak followed by a sharp, deep descent with a rapid rise back to baseline, akin to an upside-down shark dorsal fin.

Table 1. Demographics and Sleep Study Metrics

Characteristic	Value
Number of subjects	25
Age, y	
Mean ± SD	54 ± 10.38
Range	34-71
Sex	
Male (%)	21 (84%)
Female (%)	4 (16%)
BMI, kg/m^2	
Mean ± SD	30.81 ± 4.84
Range	24.39-41.60
AHI	
Mean ± SD	48.72 ± 34.38
Range	16.60-178.00
O_2 nadir (%)	
Mean ± SD	78.44 ± 6.75
Range	62.00-91.00

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; SD, standard deviation.

NP waveform shape versus pressure minimum ($P < .001$), pressure amplitude ($P < .001$), pressure slope maximum ($P < .001$), pressure slope minimum ($P < .001$), and pressure slope amplitude ($P < .001$); as well as OP waveform shape versus pressure minimum ($P < .001$), pressure amplitude ($P < .001$), pressure slope maximum ($P = .015$), pressure slope minimum ($P = .012$), and pressure slope amplitude ($P = .006$). Post hoc testing could not be performed due to the absence/limited number of observations of certain waveform shapes (ie, cycloid and shark fin waveforms in NP pressure recordings, and gentle and peak-col-hill waveforms in OP pressure recordings).

Favorable waveform shape (as highlighted in Table **3**) was associated with favorable collapse pattern on endoscopy for HGNS implantation ($P = .043^{\dagger}$). Favorable waveform shape was also associated with overall surgical candidacy for HGNS ($P = .004$).

Discussion

This pilot study demonstrates the promise of pharyngeal pressure measurement as a useful adjunct to DISE in surgical planning for patients with OSA. Waveform shape correlated with endoscopic collapse patterns for various key findings, including presence and extent of palatal collapse, direction of collapse and anatomical site of collapse below the palate, and presence and extent of collapse at the lateral oropharyngeal wall/tonsils, base of tongue, and supraglottis. Additionally, pressure amplitude and slope increase with increasing extent of collapse. Most importantly, waveform shape was significantly associated with favorable collapse patterns and overall surgical candidacy for HGNS. These findings are promising for the use of pharyngeal pressure catheters in further refining surgical candidacy selection, with the ultimate goal to improve surgical outcomes.

DISE itself, while useful, remains subjective, and results are difficult to codify given the lack of a universally accepted scoring system.[25,26] Pressure measurements with pharyngeal catheters provide an avenue to objectify these endoscopic findings. Pharyngeal pressure catheters have been used to evaluate the dynamic airway in a wide range of prior studies, during both natural sleep as well as DISE.[17,27-33,35,42-46] Several studies show the catheters are well-tolerated, safe, and do not affect sleep quality or OSA severity.[31,42,44-46]

However, this technology has yet to be leveraged to its full capacity. Older studies have largely focused on binary results, such as obstruction or no obstruction, or identifying a single site of narrowing as opposed focusing on multilevel collapse with each site of collapse incrementally contributing to airway resistance.[17,27,32] More recent work by Tvinnereim et al and Azarbarzin et al has expanded the horizons for pharyngeal pressure and related flow measurement, showing particular pressure or flow patterns can signal particular sites of collapse, helping direct the anatomic focus of surgical intervention.[34,35,47] Tvinnereim, et al exemplified the value of pharyngeal pressure recording in improving surgical outcomes in the particular case of surgical candidacy for plasma RFA.

The present study is particularly promising for pharyngeal pressure measurement in that we show its potential to not just identify presence or absence of collapse, but also determine site, extent, and direction of collapse in the OSA airway. Future directions include larger studies, assessing pharyngeal pressure for candidates for a broader range of sleep apnea interventions. Additionally, we hope to study pressure before and after intervention, to stratify pressure characteristics of treatment responders and nonresponders. With these future directions and further refinement, pressure analysis could be used as an objective tool to guide surgical selection for a variety of upper airway procedures. Furthermore, it is a futuristic yet conceivable notion to imagine pharyngeal pressure measurement in conjunction with natural sleep polysomnography (PSG) yielding the necessary information to design an individualized treatment plan for a patient with OSA, bypassing the need for a DISE, and thereby sparing the patient a procedure and streamlining their care.

Limitations of this study include the pressure catheter technology, subjective categorization of waveform shapes, and the broad statistical analysis of a small sample. The pressure catheter used contains only a single transducer, so it had to be advanced under endoscopic visualization when taking measurements in different parts of the airway. Multitransducer catheters are available but are cost-prohibitive. However, a multitransducer catheter would provide additional data as well as better standardization between patients as the catheter could be left in

Table 2. Statistical Tests

Comparison	Statistical test	Pressure measurement location	Variable 1		Variable 2		Endoscopic collapse location	*P* value (significance level = 0.05)	Bonferroni-corrected significance level
Waveform shape vs endoscopic collapse pattern	Fisher's exact test	NP	Waveform shape	vs	Presence (of collapse)	at	V	.259	0.004
				vs	Extent (of collapse)	at		.001	
				vs	Direction (of collapse)	at		.717	
		OP	Waveform shape	vs	Presence	at	O	.011[a]	
				vs	Extent	at		.022[a]	
				vs	Direction	at		.011[a]	
			Waveform shape	vs	Presence	at	T	.005[a]	
				vs	Extent	at		.037[a]	
				vs	Direction	at		.153	
			Waveform shape	vs	Presence	at	E	<.001	
				vs	Extent	at		<.001	
				vs	Direction	at		<.001	
Pressure metrics versus endoscopic collapse pattern	ANOVA	NP	Pressure amplitude	vs	Presence	at	V	.002	0.006
				vs	Extent	at		<.001	
			Pressure slope	vs	Presence	at		.133	
				vs	Extent	at		.014[a]	
		OP	Pressure amplitude	vs	Presence	at	O, T, E	.258	
				vs	Extent	at		.093	
			Pressure slope	vs	Presence	at		.529	
				vs	Extent	at		.018[a]	
Waveform shape versus pressure metrics	ANOVA	NP	Waveform shape	vs	Pressure amplitude			<.001	0.013
				vs	Pressure slope			<.001	
		OP	Waveform shape	vs	Pressure amplitude			<.001	
				vs	Pressure slope			.006	
Waveform shape (favorable status) vs favorable collapse status/HGNS candidacy	Fisher's exact test	NP or OP	Favorable waveform status	vs	Favorable collapse status			.043[a]	0.025
				vs	HGNS candidacy			.004	

Gray highlight: Significant without Bonferroni correction.

Abbreviations: ANOVA, analysis of variance; E, epiglottis (supraglottis); HGNS, hypoglossal nerve stimulator; NP, nasopharynx; O, oropharynx (lateral oropharynx and tonsils); OP, oropharynx; T, tongue (base of tongue); V, vellum (palate).

[a]Not significant after Bonferroni correction.

Table 3. Waveform Shapes and Most Common Corresponding Collapse Patterns

Measurement site and collapse pattern	Waveform shape							
	Gentle	Sinusoidal	Ramp	Cycloid	Square	Peak-plateau	Peak-col-hill	Shark fin
NP								
Presence	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Site	(Palate)	(Palate)	(Palate)		(Palate)	(Palate)	(Palate)	
Extent	Incomplete	Incomplete	Complete		Complete	Complete/ incomplete[a]	Complete	
Direction	AP	AP	AP		Mixed	AP	AP	
OP								
Presence	N/A	Yes	Yes	Yes	Yes	Yes	N/A	Yes
Site		Tonsils	BOT	Tonsils and BOT[a]	BOT	Supraglottis		Supraglottis
Extent		Incomplete	Incomplete	Incomplete	Incomplete	Incomplete		Complete
Direction		Lateral	AP	AP and Lateral[a]	AP	AP		AP

Gray highlight: Favorable waveform shape.
Abbreviations: AP, anteroposterior; BOT, base of tongue; N/A, not applicable (waveform shape not observed at this measurement site); NP, nasopharynx; OP, oropharynx; Tonsils, tonsils and lateral oropharyngeal walls.
[a]Equal distribution.

position after initial placement instead of needing to move it around. Still, the ability to move the single-transducer catheter meant measurements were taken at well-defined positions in each patient's airway, rather than some standard spacing that would not strictly correlate to each patient's anatomy. The pressure transducer also does not provide directionality, and this remains a hurdle for pharyngeal pressure transducers in general, but we were able to show at least in particular sites that waveform pattern can help identify direction of collapse.

Regarding waveform shape, visual analysis provided 8 broad categories, but admittedly this is subjective and the replicability is debatable. We believe the 8 archetypical categories were straightforward to distinguish, as we were able to quickly identify different waveform shapes even in real-time during DISE in the operating room. The statistical significance of ANOVA analysis comparing our categorical designations of waveforms with the pressure metrics bolsters this belief. Fourier analysis could help further objectify the pattern analysis. However, we caution readers to jump to Fourier analysis or other computational categorization of pressure tracings, as humans are faster and more adept at visual pattern recognition than computers in most cases.[48,49] There are several examples in medicine where we rely on our own visual pattern recognition, occasionally with the assistance of certain metrics: electroencephalography, electrocardiography (EKG), and even additional components of PSG. While EKG machines often produce automated interpretations, these are often inaccurate.[50-52] Still, this level of data processing and automated flow is an enticing future step for pharyngeal pressure tracings. The area is ripe for machine learning, and future studies with a larger patient cohort could yield a large enough data pool for further objectifying the waveform analysis.

While Bonferroni's correction may suggest many of the findings may not be significant, it is important to keep in mind that this is a small pilot study intentionally looking at many variables. This study does clearly identify parameters with the potential to be characterized using pharyngeal pressure waveforms and, as such, are worthy of further investigation. Future studies with a larger sample size and targeted statistical analysis are likely to yield results that more easily reach significance thresholds.

While this study focused on DISE and surgical candidacy, our ultimate goal entails analyzing pressure tracings with postsurgical outcomes, in efforts to assess the utility of pharyngeal pressure measurement in refining surgical selection. Another potential direction includes validation of DISE as a proxy to natural sleep, by comparing patients' pressure tracings in natural sleep PSG and to their pressure tracings during DISE.

Conclusion

Pharyngeal pressure tracings can be categorized into characteristic waveform shapes. These different characteristic waveforms are associated with different airway collapse patterns. Specifically, pressure waveform shape is significantly associated with HGNS candidacy. Upper airway pressure measurement is therefore promising as a useful adjunct to DISE in the sleep surgery candidacy evaluation.

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Author Contributions

Ravi R. Shah, study design, data acquisition, analysis, manuscript drafting/editing, accepts responsibility for the manuscript; **Ahmad F. Mahmoud**, study design, data acquisition, analysis, manuscript drafting/editing; **Raj C. Dedhia**, study design, data acquisition, manuscript drafting/editing; **Erica R. Thaler**, study design, data acquisition, manuscript drafting/editing.

Disclosures

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Supplemental Material

Additional supporting information is available in the online version of the article.

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