Patterns of Upper Airway Obstruction on Drug-Induced Sleep Endoscopy in Patients with Sleep-Disordered Breathing with AHI <5

Sam Spinowitz, MD¹, Mimi Kim, ScD², and Steven Y. Park, MD¹

Abstract

Objective. To describe the patterns of upper airway obstruction in patients with sleep-disordered breathing with apnea-hypopnea index (AHI) <5 using drug-induced sleep endoscopy (DISE).

Study Design. Retrospective study.

Setting. Tertiary care center.

Subjects and Methods. Inclusion of patients with sleep-disordered breathing with AHI <5 on polysomnography who underwent DISE. Patients <18 years of age were excluded. DISE findings were reported with the VOTEL classification system: the level of collapse was described as occurring at the velum, oropharynx, tongue base, epiglottis, and the lingual tonsils. The degree of collapse was reported as complete, partial, or none. The pattern of the obstruction was described as anteroposterior, lateral, or concentric when applicable.

Results. A total of 54 patients with sleep-disordered breathing with AHI <5 underwent DISE. Ages ranged from 19 to 65 years. DISE was performed alone in 7% (n = 4) of patients and in conjunction with surgery in 93% (n = 50) of patients. The velum was the most frequent site of upper airway obstruction (85%, n = 46), followed by base of tongue (63%, n = 34), epiglottis (39%, n = 21), lingual tonsils (35%, n = 19), and oropharynx (31%, n = 17). Eighty-three percent (n = 45) of patients had multiple levels of upper airway obstruction, and 15% (n = 8) had a single level of upper airway obstruction.

Conclusion. Patients with sleep-disordered breathing with AHI <5 have significant upper airway obstruction as seen on DISE. DISE findings indicate that a majority of these patients have multiple levels of upper airway obstruction, which can lead to significant symptoms.

Keywords
drug-induced sleep endoscopy, sleep-disordered breathing, upper airway resistance syndrome, normal AHI, upper airway obstruction

Received May 9, 2017; revised May 9, 2017; accepted June 28, 2017.

Sleep-disordered breathing (SDB) corresponds to a large spectrum of sleep disorders that can be classified into 2 main categories: patients with upper airway resistance syndrome (UARS) and patients with obstructive sleep apnea (OSA). Polysomnography remains the gold standard in differentiating between patients with OSA and UARS based on apnea-related events. Patients with SDB with an apnea-hypopnea index (AHI) <5 on polysomnography are classified as having UARS whereas those with AHI >5 are classified as having OSA. The quantitative nature of polysomnography, however, does not routinely correlate with the severity of symptoms or examination findings. Studies have demonstrated that patients with UARS are more likely to suffer from chronic insomnia when compared with patients with OSA, who have fast sleep onset. Additionally, when compared with patients with OSA, patients with UARS have been shown to have worse sleep quality, mood, and sustained attention based on well-documented surveys.
UARS, which was first described in 1993 by Guilleminault, is characterized by the complaint of excessive daytime sleepiness and frequent awakenings during sleep due to increased respiratory effort. The prevalence of UARS in the general population is documented to be approximately 10%. Patients with UARS are often misdiagnosed as having chronic fatigue syndrome, fibromyalgia, or psychiatric disorders. This causes a delay in diagnosis and mismanagement of many of these patients.

Over the past decade, drug-induced sleep endoscopy (DISE) has become an invaluable tool in the evaluation of patients with SDB. DISE was first described by Croft and Pringle in 1991. DISE involves the use of a flexible nasopharyngoscope to evaluate the upper airway during a drug-induced sleep state. In contrast to polysomnography, DISE aims to provide a more direct assessment of the behavior of patients’ upper airway anatomy during sleep. Ideally, treatment options for patients with SDB can be tailored per their unique anatomy. Most reports showing the utilization of DISE in the management of patients with SDB have been performed only in patients with OSA. Few studies have reported the utility of DISE on the management of patients with UARS specifically. We hypothesize that DISE can identify significant anatomic obstruction in patients with UARS that is not identified by conventional polysomnography parameters.

The primary aim of this study is to describe the patterns of upper airway obstruction seen on DISE with a well-documented classification system in a large cohort of patients with UARS. In doing so, this study aims to better understand upper airway dynamics in this select group of patients during sleep.

**Materials and Methods**

**Study Design**

This study was approved by the Institutional Review Board (2016-6117). This was a retrospective study of 54 patients who underwent DISE as part of their evaluation and management for SDB between January 2, 2014, and Jan 1, 2017. Patient medical records were reviewed per the surgical coding for DISE. Less than 10% of patients who had DISE during this period were included in the study. Exclusion criteria included patients <18 years of age, as pediatric OSA is scored differently on polysomnography compared to adults. Exclusion criteria also included pregnant women and allergy to propofol or to components of propofol, such as egg lecithin or soybean oil. Polysomnography was performed prior to all DISE evaluation, either in the laboratory or at home. Polysomnography was performed a median 3 months prior to DISE evaluation. Before DISE, patients were evaluated by a single ear/nose/throat sleep surgeon, with a detailed history of symptoms and physical examination, including office endoscopy.

**Drug-Induced Sleep Endoscopy**

DISE was performed by an experienced sleep surgeon, board certified in both otolaryngology and sleep medicine in an ambulatory surgery center. DISE was performed solely as a diagnostic procedure or in conjunction with a surgical procedure of the upper airway. Surgery included nasal, oropharyngeal, and hypopharyngeal procedures. Patients were placed in the supine position. Both nostrils were sprayed with 2 to 3 puffs of topical anesthetic, oxymetazoline, 10 minutes prior to starting the procedure. Glycopyrrolate was given sporadically in a handful of patients. Sedation into a deep sleep-like state was induced by a combination of the following: administration of intravenous propofol infusion, slowly titrated (starting at 50 mcg/kg/min), with 10- to 20-mg boluses as needed, based on a protocol described by Kezirian et al. At the appropriate level of sedation, the patient was breathing spontaneously in deep sleep. Care was taken to avoid inducing central apneas. A BIS monitor (bispectral index; Medtronic, Minneapolis, Minnesota) was used initially in some patients but was not as used consistently in later patients, since the BIS level of sedation did not correlate with the clinical picture.

Once the patient was in a satisfactory level of sedation, with vigorous spontaneous respiration, a 3.7-mm flexible fiberoptic endoscope coated with anticondensate was introduced into nasal cavity to visualize the nasal passageways, nasopharynx, velum, oropharynx, tongue base, epiglottis, and lingual tonsils. The areas of obstruction during the sleep state were reported with the VOTE classification system: velum, oropharynx, tongue base, and epiglottis, including the lingual tonsils. The degree of collapse was reported as complete, partial, or none. The pattern of the obstruction was described as anteroposterior, lateral, or concentric when applicable. Upper airway obstruction was categorized as either unilevel or multilevel collapse. During the procedure, jaw thrust was performed to assess the extent of base of tongue and epiglottic opening, to assess for candidacy for mandibular advancement devices or surgical options. Presence of medexpiratory palatal obstruction was also noted during DISE. All DISE findings were dictated in the operative note and used for data analysis. Video was not used for data analysis for this study.

**Statistical Analysis**

Means with standard deviations were calculated to describe baseline subject characteristics, including body mass index, AHI, and age. One-way analysis of variance tests, as well as a generalized estimating equation modeling approach with logit link, were used to assess statistical significance, estimate odds ratios, and account for the correlation in repeated measures from the same patient in the analysis of the associations between patient characteristics, including age, body mass index (BMI), AHI, and prior airway surgery, and the degree and site of upper airway obstruction.

**Results**

Patient characteristics are presented in Table 1. The study sample consisted of 54 patients: 30 women and 24 men. Ages ranged from 19 to 64 years (37 ± 12). BMI ranged from 17 to 43 (26 ± 5). AHI ranged from 0 to 5 (2.1 ± 1.5). The most common presenting symptom was chronic nasal...
congestion (66%), followed by snoring (35%). Other presenting symptoms included fatigue, migraines, and insomnia.

Thirty-nine percent (n = 21) of patients had some type of upper airway surgery in the past from an outside institution and presented with persistent symptoms.

DISE was performed alone in 7% (n = 4) of patients and in conjunction with surgery in 93% (n = 50). The most common types of surgical procedures performed with DISE were nasal procedures, followed by oropharyngeal and hypopharyngeal procedures. Nasal procedures included inferior turbinate reduction (n = 40), nasal vestibular stenosis repair (n = 31), and septoplasty (n = 27). Oropharyngeal procedures included tonsillectomy and adenoidec- tomy (n = 9) and uvulopalatopharyngoplasty (n = 7). Hypopharyngeal procedures included epiglottoplasty/supraglottoplasty (n = 7), lingual tonsillectomy/tongue base resection (n = 2), and hyoid suspension (n = 2; Figure 1).

The velum was the most frequent site of upper airway obstruction (85%, n = 46), followed by base of tongue (63%, n = 34), epiglottis (39%, n = 21), lingual tonsils (35%, n = 19), and oropharynx (31%, n = 17; Figure 2). The velum, tongue base, and epiglottis had more complete obstruction, whereas the oropharynx had more partial obstruction (Figure 3). Eighty-three percent (n = 45) of patients had multiple levels of significant upper airway obstruction, and 15% (n = 8) of patients had a single level of significant upper airway obstruction. One patient had no upper airway obstruction (Figure 4). Of those with velum

### Table 1. Patient Characteristics.

| Characteristic                  | Mean ± SD | Range     |
|--------------------------------|-----------|-----------|
| Age, y                         | 37 ± 12   | 19-64     |
| Body mass index, kg/m²         | 24 ± 5    | 17-43     |
| Apnea-hypopnea index           | 2.4 ± 1.6 | 0-5       |

*Women, n = 30; men, n = 24.

![Figure 1](image1.png)  
**Figure 1.** The operative procedure sheet for all patients included in the study. These procedures were performed immediately following the sleep endoscopy. UPPP, uvulopalatopharyngoplasty.

![Figure 2](image2.png)  
**Figure 2.** The distribution of sites of upper airway obstruction for all patients included in the study. The upper airway sites were defined with the VOTEL classification system: velum, oropharynx, tongue base, and epiglottis, including lingual tonsils.

![Figure 3](image3.png)  
**Figure 3.** The distribution of the degree of upper airway obstruction for all patients at each site. The degree of obstruction was categorized as complete or partial.

![Figure 4](image4.png)  
**Figure 4.** The patterns of upper airway obstruction for all patients were categorized as multilevel obstruction, unilevel obstruction, or none. Multilevel obstruction is defined as ≥2 sites of upper airway obstruction.
Table 2. Predictors of Obstruction from Generalized Estimating Equation Model with Logit Link.

| Variable         | Unadjusted OR (95% CI) | P Value | Adjusted OR (95% CI) | P Value |
|------------------|------------------------|---------|----------------------|---------|
| Age^a            | 0.99 (0.97-1.01)       | .19     | 0.98 (0.96-1.01)     | .15     |
| BMI^a            | 1.02 (0.98-1.06)       | .42     | 1.02 (0.97-1.07)     | .45     |
| AHI^a            | 0.88 (0.78-1.01)       | .07     | 0.86 (0.73-1.00)     | .05     |
| Prior surgery^b  | 1.43 (0.96-2.12)       | .08     | 1.55 (0.92-2.62)     | .10     |
| Site V vs E      | 9.04 (3.28-24.92)      | <.001   | 9.57 (3.41-26.91)    | <.001   |
| O vs E           | 0.72 (0.31-1.68)       | .45     | 0.70 (0.29-1.68)     | .42     |
| T vs E           | 2.67 (1.30-5.49)       | .008    | 2.76 (1.31-5.81)     | .01     |

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; E, epiglottis; O, oropharyngeal; OR, odds ratio; T, tongue base; V, velum.
^aPer unit increase.
^bYes vs no.

Discussion

This study is the first to clearly demonstrate that patients with UARS have significant levels of upper airway obstruction on DISE. Furthermore, this study demonstrates that patients with UARS have multiple levels of upper airway obstruction on DISE, which can cause significant symptoms.

Patterns of upper airway obstruction on DISE in patients with OSA have been well documented. Vroegop et al performed DISE on a cohort of 1249 patients with SDB. Twelve separate 1-way analysis of variance tests demonstrated that AHI, BMI, and age were not significantly associated with the degree of upper airway obstruction (all P values > .05) at any of the VOTE subsites. A generalized estimating equation modeling approach demonstrated that site was the only variable that was significantly associated with obstruction. The large odds ratio for “V vs E” indicates that the odds for having an obstruction is 9 to 10 times higher in the velum than the epiglottis (Table 2).

Interestingly, a number of subjects in this study had persistent and severe multilevel obstruction despite aggressive prior surgical therapy, which included maxillomandibular advancement and transpalatal advancement. In some of these patients, the AHI dropped from severe to normal levels, but symptoms returned after a short period of subjective improvement. Investigators have postulated that these patients have a central or “neurologic” etiology to their persistent symptoms. Contrarily, our study suggests that these patients have persistent upper airway obstruction despite having a “normal” AHI. Many of these patients’ symptoms improved after correction of their residual site of obstruction.

Besides retropalatal and retrolingual collapse, our study of patients with UARS saw very high rates of epiglottic obstruction. Epiglottic collapse during sleep has been estimated to occur in 12% of adult patients with OSA. Epiglottic collapse has become increasingly diagnosed in patients with OSA since the advent of DISE. Prior to DISE, the diagnosis of epiglottic obstruction was often made for patients who were nonresponders to initial soft palate surgery. Management of adult laryngomalacia is controversial, but there is a consensus that surgical therapy is usually required. In rare cases, epiglottic obstruction was seen during awake office endoscopy, but the majority were seen only during DISE. Large lingual tonsils were also seen occasionally.

While a number studies have demonstrated the effectiveness of various surgical procedures and devices for the treatment of patients with OSA, the optimal treatment of patients with UARS remains highly controversial. This is in part due to the lack of a comprehensive knowledge behind the pathophysiology of UARS and how it differs from OSA. Currently, there are no randomized controlled trials evaluating surgical treatment for UARS. Furthermore, most studies about surgery treatment consider only subjective outcomes, and the number of patients has been too low to lead to conclusive results. As a result, many surgical treatment options that are considered gold standard for use in patients with OSA, including uvulopalatopharyngoplasty, are not routinely used for patients with UARS. Most specialists in sleep medicine and
primary care recommend conservative lifestyle modifications as well as continuous positive airway pressure and oral appliances for patients with UARS. Our study suggests that patients with UARS may benefit from targeted surgical management of their symptoms.

An interesting phenomenon involving the soft palate was also observed during this study. During midnasal exhalation, the redundant soft palate will retroflex into the nasopharynx causing sudden obstruction, leading to transient breath holding and then sudden oral air release. In some cases, the breath-holding episode (similar to a mild Valsalva) is interpreted on polysomnography as a central apnea, since there is no nasal or oral airflow, as well as no respiratory effort. One patient underwent injection snoreplasty with sodium tetradecyl sulfate in the office with resolution of her expiratory palatal obstruction symptoms. A retrospective review of a series of patients with this condition is currently in progress.

This study had several limitations. While DISE has become an invaluable tool in the workup of patients with SDB, it is does not induce REM sleep, which is when upper airway obstruction is usually most severe. However, a study comparing endoscopic findings during natural sleep with those obtained during drug-induced sleep yielded basic agreement regarding the location of collapse. Furthermore, DISE requires very precise sedation anesthesia, which can vary in protocol depending on the anesthesiologist performing the sedation. In our study, most subjects were undersedated in general, with strong respiratory effort. If oversedated, there would be minimal to no respiratory effort.

In addition to those already outlined, this study has other limitations. It was a retrospective study of a small patient population. Selection bias was unavoidable, as <10% of all patients undergoing DISE during this period were included in this study. Furthermore, it was difficult to control for sleep study variability, as a mix of in-laboratory and home sleep studies, and no standardized method of standardizing sleep studies could be performed. However, all patients had documented AHI <5. A larger prospective study with a control population is needed to address these limitations and better assess upper airway dynamics in patients with UARS. A control population would include patients who undergo DISE and have no sleep symptomatology as well as a normal sleep study.

**Conclusion**

This study is the first to describe patterns of upper airway obstruction in patients with UARS on DISE. These patients have significant and multiple levels of upper airway obstruction on DISE, which can cause severe symptoms. This may explain impressive subjective improvement in some patients who snore heavily when treated surgically or with oral appliances despite having a “negative” sleep study. Studies evaluating the surgical outcomes of patients with UARS who undergo sleep surgery targeted at sites of upper airway obstruction found on DISE can potentially help elucidate better treatment options for these patients.

**Author Contributions**

Sam Spinowitz, reviewed medical records, developed a patient database, contributed to the writing/editing of manuscript, presented data; Mimi Kim, made contributions to acquisition, analysis, and interpretation of data, helped draft the statistical analysis portion and tables of the paper, approved the final version to be published, and is in agreement to be accountable; Steven Y. Park, evaluated patients in clinic and operating room, contributed to writing/editing of manuscript.

**Disclosures**

**Competing interests:** None.

**Sponsorships:** None.

**Funding source:** None.

**References**

1. Chaudhary B, Speir W Jr. Sleep apnea syndromes. *South Med J.* 1982;75:39-45.
2. Pasha R, Golub JS. *Otolaryngology–Head and Neck Surgery: Clinical Reference Guide.* San Diego, CA: Plural Publishing; 2013.
3. Anttalainen U, Tenhunen M, Rimpila V, et al. Prolonged partial upper airway obstruction during sleep—an underdiagnosed phenotype of sleep-disordered breathing. *Ear Clin Respir J.* 2016;3:31806.
4. Guilleminault C, Palombini L, Poyares D, Chowdhuri S. Chronic insomnia, premenopausal women and sleep disordered breathing: part 2. Comparison of nondrug treatment trials in normal breathing and UARS post menopausal women complaining of chronic insomnia. *J Psychosom Res.* 2002;53:617-623.
5. de Godoy LB, Luz GP, Palombini LO, et al. Upper airway resistance syndrome patients have worse sleep quality compared to mild obstructive sleep apnea. *PloS One.* 2016;11: e0156244.
6. So SJ, Lee HJ, Kang SG, Cho CH, Yoon HK, Kim L. A comparison of personality characteristics and psychiatric symptomatology between upper airway resistance syndrome and obstructive sleep apnea syndrome. *Psychiatry Investig.* 2015;12:183-189.
7. Strohs RA, Knaack L, Blum HC, Janicki J, Hohenhorst W. Differences in clinical features of upper airway resistance syndrome, primary snoring, and obstructive sleep apnea/hypopnea syndrome. *Sleep Med.* 2008;9:121-128.
8. Guilleminault C, Strohs R, Clerk A, Cetel M, Maistros P. A cause of excessive daytime sleepiness: the upper airway resistance syndrome. *Chest.* 1993;104:781-787.
9. Pepin JL, Guillot M, Tamisier R, Levy P. The upper airway resistance syndrome. *Respiration.* 2012;83:559-566.
10. Gold AR, Dipalo F, Gold MS, O’Hearn D. The symptoms and signs of upper airway resistance syndrome: a link to the functional somatic syndromes. *Chest.* 2003;123:87-95.
11. De Corso E, Fiorita A, Rizzotto G, et al. The role of drug-induced sleep endoscopy in the diagnosis and management of obstructive sleep apnoea syndrome: our personal experience. *Acta Otorhinolaryngol Ital.* 2013;33:405.

12. Vroegop AV, Vanderveken OM, Boudewyns AN, et al. Drug-induced sleep endoscopy in sleep-disordered breathing: report on 1,249 cases. *Laryngoscope.* 2014;124:797-802.

13. Croft CB, Pringle M. Sleep nasendoscopy: a technique of assessment in snoring and obstructive sleep apnoea. *Clin Otolaryngol Allied Sci.* 1991;16:504-509.

14. Bao G, Guilleminault C. Upper airway resistance syndrome—one decade later. *Curr Opin Pulm Med.* 2004;10:461-467.

15. Kezirian EJ, Hohenhorst W, de Vries N. Drug-induced sleep endoscopy: the VOTE classification. *Eur Arch Otorhinolaryngol.* 2011;268:1233-1236.

16. Viana Ada C Jr, Thuler LC, Araujo-Melo MH. Drug-induced sleep endoscopy in the identification of obstruction sites in patients with obstructive sleep apnea: a systematic review. *Braz J Otorhinolaryngol.* 2015;81:439-446

17. Ravesloot MJ, de Vries N. One hundred consecutive patients undergoing drug-induced sleep endoscopy: results and evaluation. *Laryngoscope.* 2011;121:2710-2716.

18. Torre C, Camacho M, Liu SY, Huon LK, Capasso R. Epiglottis collapse in adult obstructive sleep apnea: a systematic review. *Laryngoscope.* 2016;126:515-523.

19. Kezirian EJ. Nonresponders to pharyngeal surgery for obstructive sleep apnea: insights from drug-induced sleep endoscopy. *Laryngoscope.* 2011;121:1320-1326.

20. Metes A, Hoffstein V, Mateika S, Cole P, Haight JS. Site of airway obstruction in patients with obstructive sleep apnea before and after uvulopalatopharyngoplasty. *Laryngoscope.* 1991;101:1102-1108.

21. Shimohata T, Shinoda H, Nakayama H, et al. Daytime hypoxemia, sleep-disordered breathing, and laryngopharyngeal findings in multiple system atrophy. *Arch Neurol.* 2007;64:856-861.

22. de Godoy LB, Palombini LO, Guilleminault C, Poyares D, Tufik S, Togeiro SM. Treatment of upper airway resistance syndrome in adults: where do we stand? *Sleep Sci.* 2015;8:42-48.

23. Woodson BT. Expiratory pharyngeal airway obstruction during sleep: a multiple element model. *Laryngoscope.* 2003;113:1450-1459.

24. Quinn SJ, Daly N, Ellis PD. Observation of the mechanism of snoring using sleep nasendoscopy. *Clin Otolaryngol Allied Sci.* 1995;20:360-364.