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Comparison of Drug-induced Sleep Endoscopy and Lateral Cephalometry in Obstructive Sleep Apnea

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Abstract

Objective—To evaluate the association between findings from drug-induced sleep endoscopy (DISE) and lateral cephalometry in obstructive sleep apnea (OSA)

Study Design—Cross-sectional

Methods—This was a consecutive series of subjects with OSA who underwent DISE and lateral cephalometry. DISE findings were characterized according to the region/degree of obstruction as well as the VOTE classification. The primary measurements from lateral cephalometry images were SNA, SNB, PNSP, PAS, and MPH, although additional airway measurements were taken. Descriptive statistics summarized DISE and lateral cephalometry findings, and chi-squared and t-tests examined potential associations between their findings.

Results—Among the 55 subjects, most demonstrated velum-related obstruction, although obstruction related to other structures was also common. Lateral cephalometry findings were within population norms with the exception of an increased MPH and decreased Airway4 and Airway5 measurements. There was little association between DISE and lateral cephalometry findings, although significant associations were identified between tongue-related obstruction and airway measurements posterior to the tongue base.

Conclusion—DISE and lateral cephalometry are largely distinct airway evaluation techniques in OSA. The use of these techniques remains complementary.

Keywords

obstructive sleep apnea; drug-induced sleep endoscopy; lateral cephalometry

Introduction

Surgical treatment of obstructive sleep apnea (OSA) is directed at specific regions and structures of the upper airway. The Cochrane Collection has emphasized the importance of determination of the pattern of obstruction in individuals with OSA considering surgery.[1]

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By addressing airway obstruction in a targeted fashion, it may be possible to tailor surgical treatment to a patient's specific pattern of obstruction—improving surgical results and/or minimizing the scope of surgical intervention and the associated risks. In this light, a major goal of surgical evaluation is identification of the pattern of obstruction in order to develop targeted, effective treatment plans. Two available surgical evaluation techniques are drug-induced sleep endoscopy (DISE) and lateral cephalometric headfilms.

DISE involves fiberoptic examination of the upper airway under conditions of spontaneous ventilation and pharmacologic sedation. This technique enables 3-dimensional characterization of specific anatomic structures involved in airway obstruction under dynamic conditions. DISE has been shown to be valid,[2, 3] reliable,[4, 5] and associated with treatment outcomes.[6–9] Lateral cephalometry utilizes a standardized lateral headfilm of the head and neck taken under standardized conditions using a cephalostat with fixed head orientation. This provides an upright, 2-dimensional image of the skeletal and soft tissue anatomy of the head and neck during wakefulness. This technique has demonstrated associations with outcomes of combined palate and hypopharyngeal procedures,[10] although it too has limitations. The objective of this study was to examine potential associations between findings of these two evaluation techniques.

Materials & Methods

This cross-sectional study enrolled a consecutive series of subjects seen in consultation in the University of California, San Francisco Department of Otolaryngology—Head and Neck Surgery by one author (EJK). All subjects were 18 years of age or older, had an apnea-hypopnea index greater than 5 on overnight sleep study, were unable to tolerate positive airway pressure therapy, and elected to undergo DISE and have a lateral cephalometric headfilm taken for diagnostic purposes. Pregnant women and those patients with a contraindication to propofol (such as allergy to propofol or eggs) were excluded. Because tonsil size of 3+ or 4+ can both make DISE interpretation challenging (primarily for determination of structures other than enlarged tonsils contributing to airway obstruction) and not be visualized on a lateral cephalometric headfilm, these subjects with markedly enlarged tonsils were also excluded.

DISE was performed on all subjects by the evaluating surgeon (EJK), as described in previous publications.[4, 5, 11, 12] Topical decongestant (oxymetazoline 0.05%) was applied to both nasal cavities, and a topical anesthetic/decongestant mixture (3mL of 1% lidocaine with 1:100,000 epinephrine in most cases) was applied to one nasal cavity. Subjects were placed in a supine position on the operating room table with lights dimmed. An intravenous infusion of propofol was used as the sole sedative agent, and the minimum dose was used to achieve the target depth of anesthesia: loss of arousal to verbal stimulation. With the onset of unconscious sedation, flexible fiberoptic examination was performed. DISE findings were characterized using the VOTE Classification.[12] This classification system evaluates the structures (Velum, Oropharyngeal Lateral Walls, Tongue, and Epiglottis) that most commonly play a role in pharyngeal airway obstruction in OSA. The severity of structure related obstruction is graded on a 3-point scale: 0, no obstruction; 1, partial obstruction; or 2, complete obstruction. Although configuration of the obstruction (anteroposterior, lateral, or concentric) is also graded, this information was not used in this study. The lateral cephalometric headfilm was taken in the majority of subjects at the University of California, San Francisco Oral Radiology Clinic in the School of Dentistry using Kodak 8000C imaging (78kV, 12mA). Images obtained at outside dental X-ray laboratories were evaluated for image quality. Digital images were created from the original X-ray films, by scanning the headfilms on a flatbed scanner and subsequently digitize the images using a cephalometric software specifically designed for orthodontics(TIOPS 2005™, Roskilde, Denmark).

Brightness and contrast were adjusted to facilitate the best landmark identification process. A total of 79 cephalometric landmarks and measurements were made using the “AirwayMes” regimen, specifically developed for this project. The measurements included those cited in the sleep surgery literature for upper airway evaluation, used traditionally in orthodontics, and others related to head posture and pharyngeal airway dimensions. The measurements cited in the sleep surgery literature were considered the primary cephalometric results of interest; they included the sella-nasion-Point A (SNA) angle, sella-nasion-Point B (SNB) angle, describing the sagittal skeletal positions of maxilla and mandible. Additionally the measurements included the distance from the posterior nasal spine-tip of palate length (PNS-P), posterior airway space (PAS, also Airway6), and mandibular plane to hyoid distance (MP-H). Of secondary interest were measurements of anteroposterior airway dimensions from the nasopharynx to vallecula, numbered from Airway1 (superior nasopharynx) to Airway5 (narrowest anteroposterior dimension behind the uvula) to Airway7 (narrowest anteroposterior dimension at the vallecula). Orthodontic measurements included the nasion-sella-articulare angle (N-S-Ar, describing the lateral cranial base angle); nasion-sella-basion angle (N-S-Ba describing the median cranial base angle); angle between nasion-sella line and tangent line of disto-superior point and disto-inferior point of C2 (NSL/OPT); angle between palatal plane and sella-nasion plane (PP/SN); angle between mandibular plane and sella-nasion (MP/SN); angle between palatal plane and mandibular plane (PP/MP); and mandibular incisor angulation relative to the mandibular plane (L1/MP).

All cephalometric measurements were analyzed as continuous measures (in mm or degree angles) and in a dichotomous fashion (normal vs. abnormal/unfavorable). Abnormal/unfavorable was defined by a measurement that was greater than 1 standard deviation away from the population means, in a direction that would compromise the airway (e.g., a reduced SNB angle suggesting mandibular a posteriorly positioned mandible or retrognathia).

All cephalometric measurements were performed by one orthodontist blinded to patient history and DISE findings (SC); a sample of 10 images were tested for inter-rater reliability by a similarly-blinded senior orthodontist (IN), and the largest discrepancy in imaging points was 1.4 mm for linear dimensions and 2 degrees for angular dimensions.

Descriptive statistics were calculated for subject demographics, sleep study data, and findings from DISE and the lateral cephalometric headfilm. Primary and secondary cephalometric measurements were compared to population data[13, 14] using t-tests. For comparison of DISE and cephalometric findings, the VOTE structures were evaluated separately. Degrees 1 and 2 obstruction were combined to reflect a contribution to obstruction, while Degree 0 was regarded as no contribution. T-tests and chi-squared tests were used to compare cephalometric measurements (when continuous or dichotomous, respectively) across DISE groups for each of the VOTE structures. T-tests were also used to evaluate an association between body mass index and DISE findings. P values less than 0.05 were considered statistically significant. As there was no single primary outcome and no previous research data, it was not possible to perform an accurate sample size estimation.

Results

Fifty-five subjects underwent DISE and had lateral cephalometric headfilms taken. Eleven percent (6/55) were female, and the age was 45.0±9.0 years (range 25–66 years). Most subjects were Caucasian (89%, 49/55), including 3 (5%) who were of Hispanic ethnicity); the remaining 11% were Asian. Body mass index was 30.0 ± 5.0 kg/m^2 (range 27.5–35.3). Sleep studies showed an apnea-hypopnea index of 42.3±25.3 events/hour (range 8.7–120) with lowest oxygen saturation 80.7±9.4% (range 56–96), and 11.0±12.1% (range 0–91.1) of sleep time spent with oxygen saturation below 90%.

DISE results are shown in Table 1. A high proportion of subjects had partial (16%) or complete (76%) airway obstruction related to the velum. Other VOTE structures contributed substantially to airway obstruction, although a minority of subjects demonstrated epiglottis-related obstruction.

The primary lateral cepahlometric headfilm results and a comparison to population means are presented in Table 2. The lateral cephalometric measurements were in general not statistically different from population means, except for an increased MPH distance and decreased Airway 4 and Airway 5 dimensions.

A large number of potential associations between DISE findings (for individual structures) and lateral cephalometric measurements were evaluated. All primary and secondary cephalometric measurements were examined, and the results for the dichotomous characterization of DISE findings (0 vs. 1/2) are presented in Table 3. Among the range of statistical tests, only three statistically significant associations were identified: two for tongue-related obstruction and one for epiglottis-related obstruction during DISE. The absolute differences in Airway 5 (1.7 mm) and Airway 6/PAS (2.7 mm) measurements between subjects with and without tongue-related obstruction represent a larger fraction of the overall measurements than the difference in Airway 2 (2.9 mm) measurement for epiglottis-related obstruction. There were no associations between the dichotomous characterization of cephalometric measurements and DISE findings, except for between tongue-related obstruction and a low Airway 5 measurement ($p = 0.03$; data otherwise not shown).

The potential associations between DISE findings and lateral cephalometric findings were examined additionally in subjects with body mass index < 30 kg/m^2 (n=24). The only statistically-significant associations were seen between oropharyngeal lateral wall-involvement on DISE and decreased Airway2 and Airway3 measurements on lateral cephalometric headfilms.

Body mass index was associated with velum-related obstruction (30.5±4.8 vs. 23.7±1.8 kg/m^2, $p = 0.01$) and oropharyngeal lateral wall-related obstruction (32.2±5.2 vs. 28.9±4.6 kg/m^2, $p = 0.02$).

Discussion

This study compares findings from DISE and lateral cephalometric headfilm analysis. In spite of a wide array of statistical testing, we found few associations between findings of the two evaluation techniques.

The two significant associations seen between tongue-related obstruction during DISE and the adjacent anteroposterior airway measurements on lateral cephalogram (Airway 5 and Airway 6/PAS) are not surprising. The evaluation techniques both examine this region of the airway, and factors that contribute to tongue enlargement or posterior displacement during wakefulness (visualized on lateral cephalometry) could reasonably contribute to tongue-related obstruction during DISE. It is notable that other measurements that have been associated with outcomes of OSA surgery, such as a narrowed SNB angle measured on the lateral cephalometric headfilm,[10] were not associated with tongue-related obstruction during DISE.

The association between Airway 2 and epiglottis-related obstruction on DISE is unexpected, as the Airway 2 measurement is in the superior nasopharynx and therefore not adjacent to the epiglottis. The most likely explanation is that this is related to the increase in Type 1 error due to a multiple comparisons issue that arises with testing so many combinations of cephalometric measurements and DISE findings; we chose to define statistical significance by a p-value less than 0.05 rather than perform a maneuver such as the Bonferroni correction (as this is controversial), but it is essential to evaluate whether the observed associations are clinically reasonable and meaningful. We propose that this association is not biologically plausible and should be rejected. Epiglottis-related obstruction has been demonstrated during DISE by multiple research groups, occurring in one-fourth of subjects in this study and a similar proportions in larger studies.[4] One advantage of DISE is the ability to identify an epiglottic contribution in individuals with OSA, and this study suggests that lateral cephalometry does not provide the same information.

There were no associations between velum-related obstruction during DISE and lateral cephalometric measurements. This may relate to the high proportion of subjects with velum-related obstruction, providing inadequate statistical power with this sample size. A number of lateral cephalometry measurements may relate to velum-related obstruction, including SNA, PNS-P, and Airway 2–5, but a larger sample with a greater number of subjects without velum-related obstruction can test these associations more definitively. It should also be remembered that the lateral headfilm analysis, as used in this study, provides only a two dimensional view of a three dimensional structure. In a previous study comparing two dimensional lateral headfilms with cone beam computed tomography, there was an association between adenoid enlargement visualized on the two imaging techniques.[15]

The subjects without velum-related obstruction (but with OSA) had lower body mass index. Because elevated body mass index is a major OSA risk factor, these subjects may be atypical and have other factors contributing to OSA, including craniofacial abnormalities that could be identified by lateral cephalometric headfilm. In the subgroup with body mass index below 30 kg/m^2, there were limited associations identified, but a larger sample may provide a more thorough analysis.

There were also no associations identified between oropharyngeal lateral wall-related obstruction during DISE and lateral cephalometry measurements. As approximately half of all subjects demonstrated oropharyngeal lateral wall-related obstruction, the lack of statistically significant associations is less likely due to sample size alone. The oropharyngeal lateral walls have demonstrated abnormalities in individuals with OSA and a potential role based on DISE findings,[16–18] but lateral cephalometry may not be well-suited to an evaluation of them. Subjects with oropharyngeal lateral wall-related obstruction in this study had higher body mass index, which is consistent with the above imaging studies.

Although both DISE and lateral cephalometry are OSA surgical evaluation techniques, they differ markedly in technique. DISE provides a 3-dimensional evaluation of the airway during unconscious sedation, often performed with individuals in the supine position, while lateral cephalometry is a 2-dimensional image performed during wakefulness with individuals in the upright sitting position. Therefore, it may not be surprising that their findings have little association. DISE has demonstrated important test characteristics such as validity[2, 3, 19, 20] and reliability[4, 5] and is associated with outcomes of palate surgery[6, 7] and mandibular repositioning appliances.[8, 9] However, DISE has important limitations, including cost, sensitivity to proper technique, and the requirement of specific expertise. Lateral cephalometry has demonstrated associations with outcomes of combined palate and hypopharyneal procedures,[10] although drawbacks include radiation exposure and the lack of studies regarding validity in OSA. To inform decisions regarding OSA treatment with surgery or oral appliances, future research should continue to examine these evaluation techniques, including their association with surgical outcomes.

There are important limitations to this study. First, a larger sample size may have identified other statistically-significant associations between DISE and lateral cephalometric measurements than were found, particularly for velum-related obstruction. Second, it is possible that different combinations of lateral cephalometric headfilm measurements may provide information not available for individual measurements. Third, there is presently no gold standard for OSA upper airway evaluation to define the pattern of obstruction, making it impossible to determine whether one of these techniques is more accurate. Future studies using 3-dimensional cone beam computed tomography analysis may provide a better understanding of the association between OSA and airway anatomy.

Conclusion

DISE and lateral cephalometric headfilm analysis do not provide similar information about airway obstruction in OSA.

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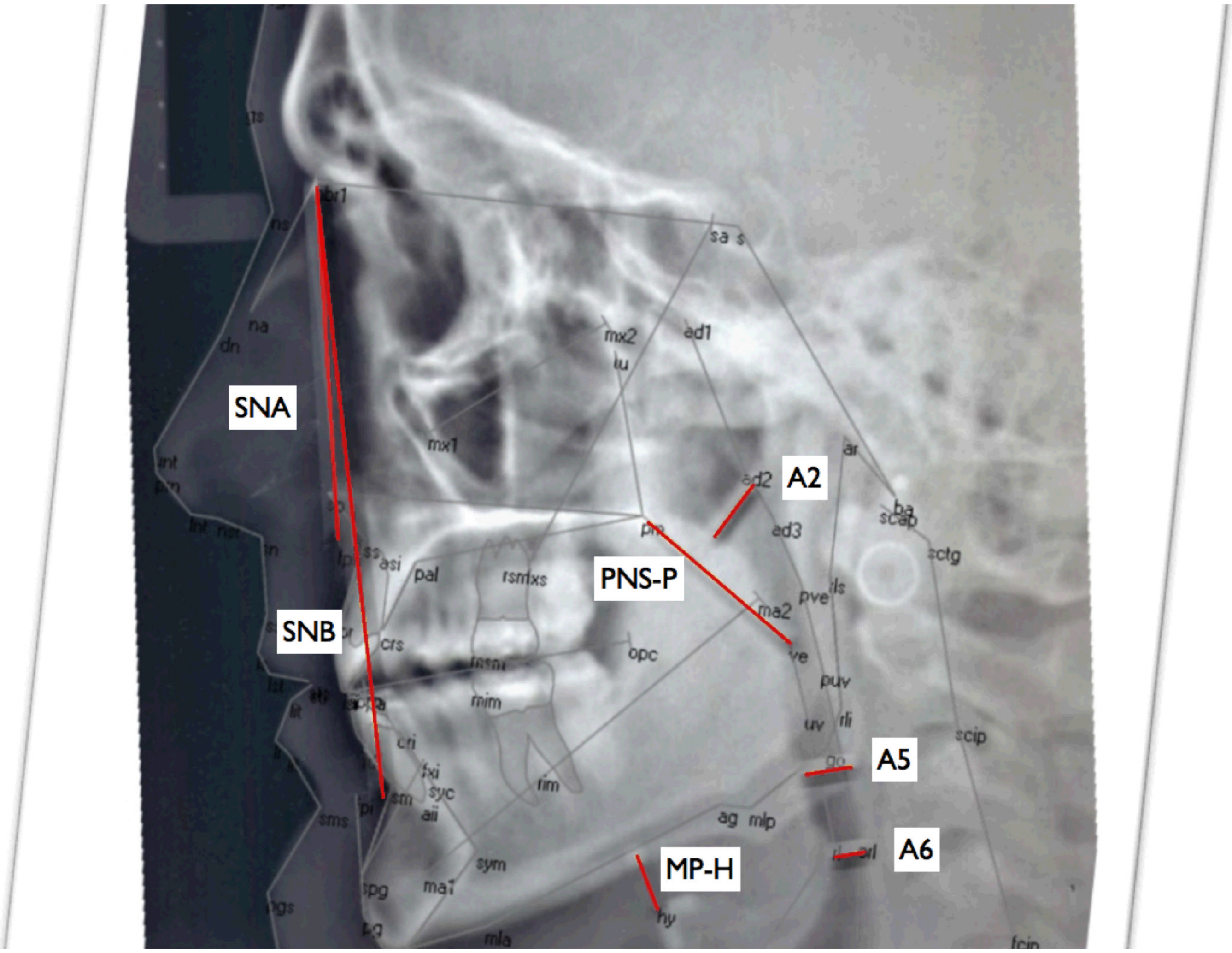

Figure 1.
Landmarks identified on lateral cephalogram.
Key: SNA, sella-nasion-Point A; SNB, sella-nasion-Point B; MP-H, mandibular plane to hyoid; PNS-P, posterior nasal spin to palate; A2, Airway2; A5, Airway5; A6, Airway6.

Table 1

DISE findings

DISE Structure	Degree of Obstruction	Frequency	Percent
Velum	0	4	7.3
	1	9	16.4
	2	42	76.4
OP lateral walls	0	28	50.9
	1	17	30.9
	2	10	18.2
Tongue	0	16	29.1
	1	17	30.9
	2	22	40.0
Epiglottis	0	42	76.4
	1	9	16.4
	2	4	7.3

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Table 2

Primary lateral cephalogram measures and comparison to population norms

Variable	Sample Mean ± SD (mm)	Population Mean ± SD (mm)[18, 19]
SNA	81.1 ± 0.66	82.0 ± 3.5
SNB	78.3 ± 0.65	80.0 ± 3.0
PNSP	39.8 ± 0.57	37.2 ± 4.7
MPH	22.5 ± 0.88 *	15 ± 2.0
PAS (Airway 6)	10.4 ± 0.55	9.30 ± 3.1
Airway 1	10.7 ± 3.3	9.1 ± 1.8
Airway 2	22.7 ± 4.5	23.2 ± 3.2
Airway 3	24.2 ± 4.2	25.7 ± 2.9
Airway 4	7.0 ± 3.4 *	10.1 ± 2.8
Airway 5	8.2 ± 2.5 *	11.8 ± 2.8
Airway 7	18.6 ± 4.7	18.6 ± 2.3

*Different from population normal values ($p < 0.05$)

Table 3

Tests of association between DISE findings and primary cephalometric measurements.

Cephalometric Measure	DISE Structure	Obstruction				*P*
		No		Yes		
		Mean	SD	Mean	SD	
SNA	Velum	79.0	3.5	81.3	0.7	0.37
	Oropharynx	81.0	5.2	81.4	4.6	0.79
	Tongue	81.7	4.4	80.9	5.2	0.56
	Epiglottis	80.5	5.2	83.3	3.2	0.11
SNB	Velum	75.3	3.8	78.6	4.8	0.19
	Oropharynx	78.5	5.2	78.0	4.1	0.71
	Tongue	79.1	5.2	78.0	4.7	0.47
	Epiglottis	78.0	4.9	79.3	4.7	0.39
PNSP	Velum	38.2	4.9	39.9	4.2	0.45
	Oropharynx	39.2	4.1	40.9	4.4	0.16
	Tongue	40.2	3.7	39.6	4.5	0.64
	Epiglottis	39.8	4.4	39.5	3.7	0.83
MPH	Velum	22.2	3.1	22.5	6.2	0.91
	Oropharynx	22.8	5.7	21.9	6.7	0.67
	Tongue	23.0	5.0	22.3	6.4	0.73
	Epiglottis	22.2	6.2	23.7	5.5	0.49
ANB	Velum	3.7	3.9	2.8	2.9	0.56
	Oropharynx	2.5	3.2	3.4	2.4	0.31
	Tongue	2.8	3.0	2.8	2.9	0.96
	Epiglottis	2.5	2.9	3.8	2.8	0.16
Airway 1	Velum	9.2	2.0	10.9	3.4	0.34
	Oropharynx	10.7	3.5	10.8	3.1	0.92
	Tongue	11.3	3.5	10.5	3.3	0.41
	Epiglottis	10.5	3.4	11.7	3.1	0.26
Airway 2	Velum	22.5	7.0	22.9	4.2	0.86

Cephalometric Measure	DISE Structure	Obstruction				P
		No		Yes		
		Mean	SD	Mean	SD	
	Oropharynx	23.5	4.2	21.6	4.6	0.12
	Tongue	22.6	4.4	22.6	4.4	0.47
	Epiglottis	22.2	4.7	25.1	2.4	0.04
Airway 3	Velum	23.0	5.9	24.5	4.0	0.48
	Oropharynx	24.7	4.3	23.6	3.6	0.35
	Tongue	24.7	2.7	24.2	4.5	0.72
	Epiglottis	23.8	4.4	26.1	1.6	0.08
Airway 4	Velum	8.1	3.4	7.0	3.4	0.54
	Oropharynx	7.2	3.2	6.9	3.8	0.78
	Tongue	7.5	3.5	6.9	3.3	0.57
	Epiglottis	7.3	3.4	6.3	3.2	0.35
Airway 5	Velum	8.5	1.9	8.1	2.5	0.79
	Oropharynx	8.2	2.4	8.1	2.7	0.90
	Tongue	9.3	2.6	7.6	2.2	0.02
	Epiglottis	8.3	2.5	7.6	2.4	0.40
Airway 6 / PAS	Velum	9.6	5.7	10.5	4.0	0.68
	Oropharynx	10.1	3.6	11.1	4.9	0.40
	Tongue	12.4	3.5	9.7	4.1	0.03
	Epiglottis	10.3	4.2	10.9	4.0	0.68
Airway 7	Velum	18.5	3.4	18.7	4.9	0.92
	Oropharynx	18.7	4.3	18.6	5.6	0.94
	Tongue	18.6	5.0	18.7	4.7	0.93
	Epiglottis	18.9	5.0	18.0	3.8	0.54
NSAR	Velum	123.8	3.6	121.4	5.6	0.41
	Oropharynx	121.3	4.9	122.1	6.4	0.60
	Tongue	122.3	5.2	121.3	5.6	0.55
	Epiglottis	121.5	5.4	121.8	5.7	0.88

Cephalometric Measure	DISE Structure	Obstruction				*P*
		No		Yes		
		Mean	SD	Mean	SD	
NSBA	Velum	128.5	3.4	125.7	6.2	0.38
	Oropharynx	125.7	5.9	126.3	6.3	0.71
	Tongue	126.3	5.0	125.7	6.5	0.76
	Epiglottis	126.2	5.8	124.8	6.8	0.46
NSLPOT	Velum	108.8	6.7	109.9	8.3	0.80
	Oropharynx	109.0	9.0	111.2	6.3	0.36
	Tongue	108.0	7.8	110.5	8.3	0.31
	Epiglottis	110.0	8.1	109.0	8.6	0.70
PPSN	Velum	7.5	3.5	7.7	4.0	0.94
	Oropharynx	7.3	4.0	8.3	3.9	0.35
	Tongue	7.1	4.4	7.9	3.8	0.50
	Epiglottis	7.9	4.0	6.9	3.8	0.43
MPSN	Velum	33.7	8.7	32.7	7.0	0.78
	Oropharynx	33.1	7.6	32.1	6.2	0.63
	Tongue	31.3	5.2	33.3	7.7	0.34
	Epiglottis	33.0	7.7	31.7	4.7	0.55
PPMP	Velum	26.2	8.3	25.0	5.8	0.70
	Oropharynx	25.8	5.9	23.7	6.0	0.23
	Tongue	24.2	5.0	25.4	6.3	0.50
	Epiglottis	25.2	6.4	24.8	4.3	0.86
L1MP	Velum	93.8	9.1	92.9	7.0	0.81
	Oropharynx	92.3	8.0	94.3	4.7	0.31
	Tongue	91.6	8.4	93.5	6.4	0.37
	Epiglottis	92.7	7.3	94.0	6.4	0.56