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AWAKE ENDOSCOPIC ASSESSMENT OF THE UPPER AIRWAY DURING TIDAL BREATHING: DEFINITION OF ANATOMICAL FEATURES AND COMPARISON WITH DRUG-INDUCED SLEEP ENDOSCOPY

Short running title: endoscopic features during tidal breathing

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Ethical considerations

The current data were obtained from a prospective trial (PROMAD)[13] that was approved by the local ethics committee at the Antwerp University Hospital and University of Antwerp (11/11/103, registration number: B300201212961). All patients gave written informed consent prior to participation. The parent study was registered on clinicaltrials.gov with identifier NCT01532050.

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Awake Endoscopic Assessment of the Upper Airway during Tidal Breathing: Definition of Anatomical Features and Comparison with Drug-induced Sleep Endoscopy

Objectives: Awake nasopharyngoscopy is routinely performed in the assessment of patients who require treatment for sleep-disordered breathing (SDB). However, the applicability and accuracy of Müller's manoeuvre, the main evaluation method for this purpose, are disputable. The current study aimed to introduce an alternative method for awake nasopharyngoscopy in patients with SDB.

Design: We defined qualitative anatomical features during tidal breathing at the levels of the soft palate, oropharynx, tongue base, epiglottis and hypopharynx, and compared these awake features to the sites and patterns of collapse as observed during drug-induced sleep endoscopy (DISE).

Setting: Tertiary care academic centre.

Participants: Seventy-three patients diagnosed with SDB.

Main outcome measures: The primary outcome measure was the Kendall's tau correlation coefficient (τ) between observations during awake nasopharyngoscopy and DISE. Kappa-statistics (κ) were calculated to assess the agreement on awake endoscopic features with a second observer.

Results: In contrast to epiglottis shape, the modified Cormack-Lehane scale was significantly associated with epiglottis collapse during DISE ($P<0.0001$; $\tau=0.45$). Other upper airway features that were correlated with DISE collapse were the position of the soft palate ($P=0.007$; $\tau=0.29$), crowding of the oropharynx ($P=0.026$; $\tau=0.32$) and a posteriorly located tongue base ($P=0.046$; $\tau=0.32$). Interobserver agreement of endoscopic features during tidal breathing was moderate ($0.60\leq\kappa<0.80$).

Conclusion: The current study introduces a comprehensive and reliable assessment method for awake nasopharyngoscopy based on anatomical features that are compatible with DISE collapse patterns.

INTRODUCTION

Endoscopic assessment of the upper airway (UA) is indispensable in clinical practice to guide therapeutic decision making in patients with sleep-disordered breathing.[1] As obstruction of the UA can occur at one or multiple levels in obstructive sleep apnoea (OSA), treatment modalities other than continuous positive airway pressure (CPAP) need to be specifically tailored to the obstruction pattern of each individual.[2] In the last two decades, drug-induced sleep endoscopy (DISE) has gained great popularity and credibility in selecting proper candidates for non-CPAP treatment.[3] DISE allows a dynamic and three-dimensional assessment of UA collapse patterns during a sedative state mimicking natural sleep.[3] However, it comes with financial and structural drawbacks, and requires adequate training and sufficient experience.[4]

The clinical examination of patients with OSA often comprises awake nasopharyngoscopy with Müller's manoeuvre (MM), a forced inspiratory effort against a closed airway.[5] However, several limitations of MM have been reported: 1) the observations are strongly dependent on the inspiratory effort of patients [6]; 2) the observed collapse patterns are not compatible with objective measurements during sleep [7]; and 3) the predictive value of MM for surgical success is insufficient.[8] Moreover, a plethora of studies have demonstrated significant incongruities between MM and DISE.[9-12]

Nevertheless, awake nasopharyngoscopy offers many advantages, including a wide accessibility, low cost, and minimally invasive nature. Thus, we aimed to increase the utility of this examination by developing a straightforward evaluation method without the need of manoeuvres executed by patients. For this purpose, we defined qualitative UA features during tidal breathing, and compared these findings to collapse patterns during DISE.

METHODS

Ethical considerations

The current data were obtained from a prospective trial (PROMAD)[13] that was approved by the local ethics committee at the Antwerp University Hospital and University of Antwerp (registration number: B300201212961). All patients gave written informed consent prior to participation. The parent study was registered on clinicaltrials.gov with identifier NCT01532050.

Participants

One hundred adult patients with diagnosis of OSA were prospectively recruited from a specialised ear, nose and throat (ENT) department in a tertiary care centre. Key exclusion criteria were body mass index (BMI) >35 kg/m², preceding UA surgery, syndromic craniofacial or UA anomalies, and history of psychiatric disorders.

At inclusion, detailed clinical information was obtained from all patients, including neck circumference, BMI,palatine tonsil grade according to Friedman, and modified Mallampati score. Polysomnography was repeated to establish a baseline diagnosis.Patients with primary snoring(apnoea-hypopnea index [AHI] <5 events/h) were not excluded in order to increase the generalisability of the findings. The severity of OSA was graded as mild (5≤ AHI <15 events/h), moderate (15≤ AHI <30 events/h), or severe (AHI ≥30 events/h). Afterwards, all patientsunderwent DISE and awake nasopharyngoscopy.

Awake nasopharyngoscopy

Awake nasopharyngoscopy was performed using a flexible fibreoptic endoscope (Olympus ENF-GP, diameter 3.7 mm, Olympus Europe GmbH, Hamburg, Germany) by an experienced ENT surgeon with patients in the upright position. No topical nasal anaesthetics or decongestants were used prior to insertion of the endoscope. The following UA levels were systematically examined during tidal breathing and MM: the soft palate, oropharynx, tongue base, epiglottis, and hypopharynx.

Endoscopic evaluation during tidal breathing was based on specific qualitative features (Figure 1). The position of the soft palate was assessed by means of three distinct shapes: (1) the 'oval shape' represented an anterior position; (2) the 'C-shape' was characterized by a prominent uvula without narrowing of the lateral sides; and (3) the 'dumbbell shape' indicated overall narrowing of the velopharynx due to a posteriorly located soft palate. Crowding of the oropharynx corresponded to large palatine tonsils or pronounced pharyngeal pillars relative to the UA dimensions. The tongue base position was assessed according to the visibility of the vallecula: 1) completely visible, 2) partially visible, 3) not visible, and 4) compression of the epiglottis and/or contact with the posterior pharyngeal wall – also referred to as a posteriorly located tongue base. The Friedman grading system was used in the evaluation of the lingual tonsils.[14] The shape of the epiglottis was described as normal (slightly concave curvature), flat, or curved (including omega-shape). Finally, assessment of the hypopharynx was based on the modified Cormack-Lehane scale: 1) vocal cords completely visible, 2) vocal cords partially visible, 3) arytenoids visible but vocal cords not visible, and 4) glottis not visible.[15]

Observations during MM were made using the same standardized scoring system as during DISE.[4] The degrees of UA narrowing were denoted as none (0-49%), partial (50-74%)or complete (≥75%).

The nasopharyngoscopic video recordings were independently reviewed by a second experienced ENT surgeon who was instructed on the scoring system as detailed above but did not receive any additional training. Scoring discrepancies between both reviewers were revised to reach consensus on the awake observations. This consensus score was used for further analysis and comparison with DISE collapse patterns.

Drug-induced sleep endoscopy (DISE)

DISE was performed by an experienced ENT surgeon in a semi-dark and silent operating theatre with patients in the supine position. Sedation was induced by an intravenous bolus injection of 1.5 mg midazolam and maintained by target-controlled infusion (TCI) of propofol (2.0–3.0 µg/ml). The sedation level was continuously assessed using 4 bispectral index (BIS) monitoring sensor electrodes (BIS VISTA monitor and BIS Quatro, Aspect Medical Systems Inc., Norwood, USA). The pursued BIS-values ranged from 50 to 70. Presence of UA collapse was noted using a standardized scoring system, specifying the corresponding level (soft palate, oropharynx, tongue base, epiglottis or hypopharynx), degree (none, partial or complete) and direction (anteroposterior, concentric or lateral).[4] Scoring of DISE was performed by a committee of four experienced ENT surgeonsat our centre. Prior to reviewing the DISE video recordings, specific definitions of collapse were established for all UA levels. Scoring discrepancies among the review members were deliberated until global consensus was reached. In cases without agreement on the level, degree or direction of UA collapse, no scores were assigned.

Statistical analysis

All data were analysed using SPSS statistics 25.0 (IBM corporation, Armonk, USA). Continuous variables are expressed as mean ± standard deviation or median (25^{th}–75^{th} percentile) unless otherwise specified. Correlations between clinical measurements, awake nasopharyngoscopy and DISE were assessed using Kendall's tau_{β} coefficient (τ). The percentage of agreement and kappa-values (κ) between reviewerswere calculated to evaluate the interobserver agreement of nasopharyngoscopic observations. Cohen's and weighted (using linear weights) κ-values were used for nominal and ordinal variables, respectively. κ-values are reported using the following strength of agreement categories: none (0–0.19), minimal (0.20–0.39), weak (0.40–0.59), moderate (0.60–0.79), strong (0.80–0.89), and almost perfect (≥0.90).[16]95% confidence intervals (95%CI) were produced using bootstrap with 1,000 iterations.A P-value of <0.05 was considered statistically significant.

RESULTS

Clinical characteristics

One patient did not complete repeat polysomnography, 16 patients did not undergo DISE, and 10 patients had no awake nasopharyngoscopy. Thus, a complete dataset was obtained in 73 patients (Table 1). Thirty-three of them (45.2%) were diagnosed with mild OSA, 23 (31.5%) with moderate OSA, and 9 (12.3%) with severe OSA. The remaining 8 patients (11.0%) showed primary snoring.Patients with primary snoring were generally less overweight (BMI 25.0 ± 2.0 kg/m² vs. 27.8 ± 3.4 kg/m²; *P*=0.004) and more often female (50.0% vs. 16.9%; *P*=0.051) than patients with OSA. There were no significant differences in age, neck circumference, and Epworth Sleepiness Scale between both groups. The AHI of the entire cohort ranged from 0 to 69.9 events/h.

Table 2 shows the distribution of observations during awake nasopharyngoscopy and DISE. At the level of the soft palate, collapse during MM occurred mainly in the lateral (30.1%) and concentric direction (34.2%), whereas collapse during DISE was more present in the anteroposterior (59.4%) than concentric (36.2%) direction.

Correlations between awake findings and DISE

Figure 2 compares both awake assessments in terms of concordance with DISE. Only complete palatal collapse during DISE was considered for analysis due to the overall high prevalence (94.5%) of collapse at this level. Four endoscopic features during tidal breathing were significantly correlated with DISE: 1) the position of the soft palate with complete palatal collapse[τ=0.29 (95%CI: 0.07–0.49); *P*=0.007]; 2) crowding of the oropharynxwith oropharyngeal collapse [τ=0.32 (0.04–0.56); *P*=0.026]; 3) a posteriorly located tongue base with complete tongue base collapse [τ=0.32 (0.04–0.60); *P*=0.046]; and 4) the modified Cormack-Lehanescalewith epiglottis collapse [τ=0.45 (0.30–0.58); *P*<0.001]. The position of the soft palate was not associated with the direction of palatal collapse during DISE. The only significant correlation between MM and DISE was found at the level of the oropharynx [τ=0.33 (0.11–0.53); *P*=0.003].

Looking at other clinical characteristics, positive correlations were found between neck circumference and complete palatal collapse during DISE [τ=0.23 (0.01–0.43); *P*=0.037], and between palatine tonsil sizeand oropharyngeal collapse [τ=0.32 (0.12–0.50); *P*=0.004]. Moreover, tongue base collapse was negatively correlated with BMI [τ=-0.24 (-0.39 to -0.04); *P*=0.010]. Neither the modified Mallampati score nor lingual tonsil size were associated with tongue base collapse.

Interobserver agreement

Both observers showed a moderate agreement for all UA features during tidal breathing (Table 3). The highest level of agreement was detected for the Cormack-Lehane scale (κ=0.73) and the lowest level for oropharyngeal crowding (κ=0.61). The interobserver agreement for UA collapse during MM, on the other hand, ranged from minimal to moderate, with highest κ-values for the soft palate (κ=0.72) and lowest κ-values for the hypopharynx (κ=0.33).

DISCUSSION

Synopsis of key findings

Although ENT specialists often intuitively evaluate the appearance of the UA using nasopharyngoscopy, the current study introduced a comprehensive and reproducible evaluation method during tidal breathing and compared these observations withcollapse patterns during DISE. Based on our results, this evaluation method enables a better correlation withcollapse patterns during DISE than the traditional assessment using MM.

Comparisons with other studies

The tonsillar grading scale is viewed by many as a reliable predictor for oropharyngeal collapse in patients with OSA.[17]Besides corroborating this perception, the current study also demonstrated a correlation between oropharyngeal crowding and oropharyngeal collapse during DISE.Both awake measures of the oropharyngeal region showed an identical correlation with DISE (τ=0.32). However, combining tonsillar hypertrophy (*i.e.* grade ≥2) and nasopharyngoscopic crowding produced a strengthened correlation with DISE collapse (τ=0.43; P=0.015). This suggests that both clinical features are complementary, with nasopharyngoscopy offering the advantage of visualizing the impact of the palatine tonsils and pharyngeal pillars on the UA lumen.

No correlations were found between the tongue base position and tongue base collapse during DISE; however, separate analysis for a posteriorly located tongue base revealed a significantcorrelation with complete tongue base collapse. This finding confirms the principle that tongue base collapse is not a direct function of tongue size and primarily depends on the relaxation of pharyngeal and lingual muscles during sleep.[10,18] Additional measures of tongue size, namely the modified Mallampatiscore and lingual tonsil grade, were also discordant with tongue base collapse observed during DISE, thereby supporting previous findings.[19,20] Interestingly, and consistentwith previous research,[21] tongue base collapse and BMI were inversely correlated.

*Torre et al.*recently adapted the modified Cormack-Lehane scale for nasopharyngoscopicassessment of the hypopharyngeal regionshowing a moderate agreement between novice and high agreement between expert reviewers.[15] For the first time, however, our study correlated this scoring system with epiglottis collapse during DISE. Additionally, we validated the reliability of the modified Cormack-Lehane scale for routine nasopharyngoscopy by using video recordings instead of still images.[15]These findings are highly relevant for clinical practice, as awake examinations are generally unable to predict epiglottis collapse, necessitating the use of more invasive examinations such as DISE.[11]

The epiglottis shape was not related to epiglottis collapse during DISE. This finding is in contrast to research of *Delakorda and Ovsenik*whofound a higher proportion of epiglottis collapse during DISE in patients with a flattened epiglottis shapethan in patients with a normal or curved shape.[22]However, the authors noticed that among patients with a flattened epiglottis, those with an anteriorly curved epiglottis edge had less risk of collapse during DISE. Thus, the discrepancy between our and their study might be attributed to the fact that we did not classify this feature of the epiglottis.

Except for oropharyngeal collapse, the current study found no correlations between MM and DISE, whichis consistent with previous research.[9-12] The accuracy of MM has also been questioned in studies using other evaluation methods to determine UA collapse such as pressure-transducer recordings during natural sleep.[7] Moreover, the effort-dependent nature of MM has been demonstrated by *Ritter et al.* who observed progressive narrowing of the retropalatal area with gradual decreases of intraluminal pressure.[6] They also noticed that changes in UA calibre occurred primarily in the lateral dimension. Since MM is an active event with recruitment of UA muscles,[23] the collapsibility of the UA may bealso reduced, thereby underestimating several types of collapse. Hence, we advocate to limit MM to pharyngeal structures with laterally oriented types of collapse (*i.e.* oropharynx).

Limitations

We acknowledge a number of potential limitations to this study. The observations during tidal breathing might have been influenced by differences in breathing route among patients. Although previous research has demonstrated equal resistance values during oral and nasal breathing in awake patients,[24] oral breathing might alter the position of the soft palate and increase the degree of mouth opening. Hence, we recommend standardizing the breathing route in future applications by instructing patients to breath quietly through the nose with the mouth closed. All patients were also examined in the upright position. However, as demonstrated in previous research,[25] the UA is generally narrower in the supine position, especially at the level of the soft palate. Therefore, UA features might be more distinct and noticeable in the supine position.

Another important limitation of thestudyis that observations of UA features during tidal breathing were averaged throughout the respiratory cycle. Nevertheless, previous research hasindicated dimensional differences in UA calibre depending on the respiratory phase.[26,27]More specifically, UA cross-sectional areas remain relatively constant during inspiration, enlarge during early expiration, and significantly narrow during late expiration. These dynamic changes are presumably secondary to pharyngeal muscle relaxation during expiration. Therefore, we strongly advise to evaluate the UA at fixed times in the respiratory cycle, preferably at end-tidal expiration, in order to optimize the reproducibility of the findings.

Lastly, we based the scoring system for awake nasopharyngoscopy on qualitative features and omitted any quantitative measurements, such as cross-sectional areas of UA levels. Nevertheless, we deemed such a qualitative assessment more appealing for clinical practice. Similarly, DISE interpretation is subjective and thus prone to intra- and interobserver variability.[4]This point of criticism, however,was tackled by using consensus scoring for both awake nasopharyngoscopy and DISE.

Clinical applicability

With the mentioned caveats in mind,nasopharyngoscopy may enhance the quality of the routine clinical examination in patients with suspected OSA by providing a minimally invasive and reliable estimation of UA collapse. The proposed evaluation system allows a comprehensive description of the anatomical levels involved in OSA.[21] Contrary to pre-existing methods, this assessment takes place during normal respiration without the need of specific manoeuvres executed by patient, thereby minimizing the impact of patient cooperation. Additionally, as the agreement with a second untrained observer was moderate for all UA features during tidal breathing, we expect this assessment to be feasible and easily translatable to clinical practice. Nevertheless, similar to other examinations during wakefulness,nasopharyngoscopy fails to appreciate changes in UA muscle tonerelated to the sleeping state. As these changes are an important contributor to OSA pathogenesis,[28]awake nasopharyngoscopy should not be regarded as a substitute forassessment methods performed during (drug-induced) sleep for deciding on (surgical) treatment. Rather, we advocate the proposedassessment method as a first-line instrument to counsel patients and guide furtherinvestigations.

CONCLUSION

The present studydemonstrated that specific nasopharyngoscopic features observed during awake tidal breathing are compatible with DISE collapse patterns. This comprehensive assessment method may provide a valuable clinical tool to describe different UA structures at the outpatient clinic.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Variables	Subjects (n = 73)
Gender (% male)	79.5
Age (years)	48.0 ± 9.7
BMI (kg/m²)	27.5 ± 3.3
Neck circumference (cm)	39.2 ± 3.2
AHI (events/h)	13.3 (8.1–22.5)
ODI (events/h)	3.4 (1.6–10.9)
Mean O_2 saturation (%)	95.3 (94.3–96.3)
Minimal O_2 saturation (%)	88.0 (84.0–90.0)

Table 1. Patient characteristics.

Data are presented as mean ± standard deviation or as median (25^{th}–75^{th} percentile). AHI = apnoea-hypopnoea index; BMI = body mass index; ODI = oxygen desaturation index.

	Awake nasopharyngoscopy				DISE collapse	
	Tidal breathing UA features		*MM collapse*			
Soft palate	Oval	46 (63.0%)	Absent	12 (16.4%)	Absent	4 (5.5%)
	C-shaped	20 (27.4%)	Partial	19 (26.0%)	Partial	34 (46.6%)
	Dumbbell	7 (9.6%)	Complete	42 (57.5%)	Complete	35 (47.9%)
Oropharynx	Normal	61 (83.6%)	Absent	32 (43.8%)	Absent	52 (72.2%)
	Narrow	12 (16.4%)	Partial	29 (39.7%)	Partial	15 (20.8%)
			Complete	12 (16.4%)	Complete	5 (6.9%)
Tongue base	Grade 1	13 (17.8%)	Absent	52 (71.2%)	Absent	32 (44.4%)
	Grade 2	15 (20.5%)	Partial	10 (13.7%)	Partial	32 (44.4%)
	Grade 3	28 (38.4%)	Complete	11 (15.1%)	Complete	8 (11.1%)
	Grade 4	17 (23.3%)				
Epiglottis	Normal	35 (47.9%)	Absent	73 (100%)	Absent	56 (78.9%)
	Flat	27 (37.0%)	Partial	0 (0%)	Partial	8 (11.3%)
	Curved	11 (15.1%)	Complete	0 (0%)	Complete	7 (9.8%)
Hypopharynx	† Grade 1	8 (11.0%)	Absent	51 (69.9%)	Absent	54 (77.1%)
	Grade 2	23 (31.5%)	Partial	19 (26.0%)	Partial	16 (22.9%)
	Grade 3	22 (30.1%)	Complete	3 (4.1%)	Complete	0 (0%)
	Grade 4	20 (27.4%)				

Table 2. Consensus scoring for awake nasopharyngoscopy and DISE.

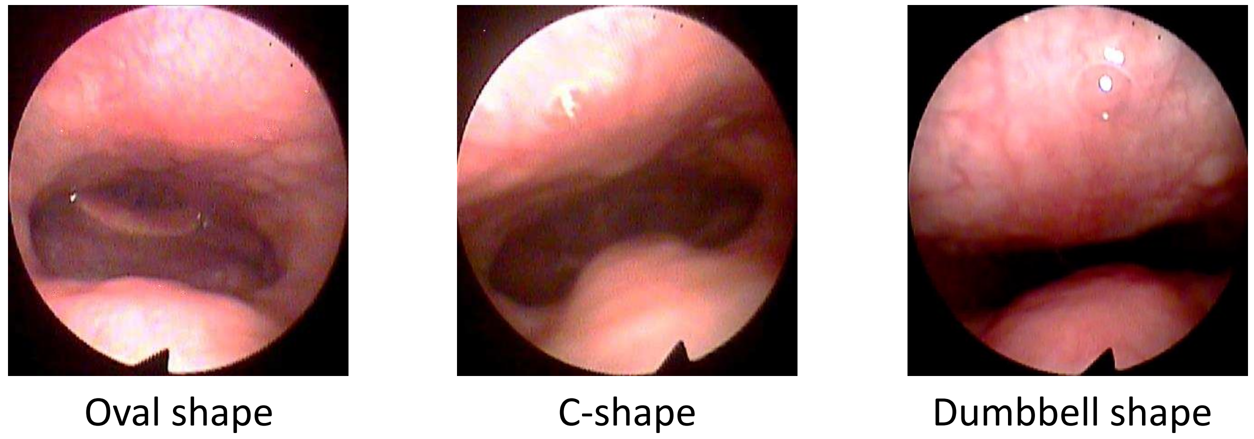
† Modified Cormack-Lehane scale. DISE = drug-induced sleep endoscopy; MM = Müller's manoeuvre; UA = upper airway.

	Observation	Rater 1 (*N*)	Rater 2 (*N*)	% agreement (95%CI)	κ value (95%CI)
	TIDAL BREATHING				
	Oval	52	47		
Soft palate	C-shape	15	20	86.3 (78.1–94.5)	0.717 (0.546–0.863)
	Dumbbell	6	6		
Oropharynx	Open	64	61	90.4 (82.2–97.3)	0.612 (0.306–0.846)
	Narrow	9	12		
	Grade 1	11	14		
Tongue base	Grade 2	19	21	68.1 (56.5–79.7)	0.680 (0.562–0.798)
	Grade 3	27	29		
	Grade 4	16	9		
	Normal	33	36		
Epiglottis	Flat	31	26	82.2 (74.0–90.4)	0.707 (0.549–0.845)
	Curved	9	11		
	Grade 1	10	11		
Modified CLS	Grade 2	18	23	73.9 (62.3–84.1)	0.730 (0.625–0.835)
	Grade 3	29	25		
	Grade 4	16	14		
	MÜLLER'S MANOEUVRE				
	Absent	11	15		
Soft palate	Partial	22	14	79.9 (69.6–88.4)	0.721 (0.585–0.856)
	Complete	40	44		
	Absent	32	32		
Oropharynx	Partial	29	28	71.0 (59.4–81.2)	0.594 (0.434–0.754)
	Complete	12	13		
	Absent	55	57		
Tongue base	Partial	6	9	79.7 (69.6–88.4)	0.542 (0.337–0.747)
	Complete	12	6		
	Absent	73	64		
Epiglottis	Partial	0	3	92.8 (85.5–98.6)	—
	Complete	0	2		

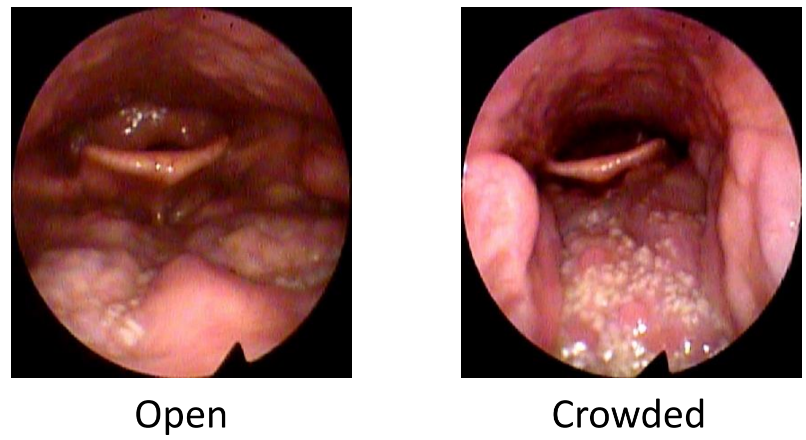
	Absent	58	40		
Hypopharynx	Partial	10	27	68.1 (58.0–78.3)	0.325 (0.144–0.506)
	Complete	5	5		

Table 3. Interobserver agreement for observations during awake nasopharyngoscopy.
The kappa (κ) value of epiglottis collapse during Müller's manoeuvre could not be calculated since all ratings of the first observer were identical. 95%CI = 95% confidence interval; CLS = Cormack-Lehane Scale.

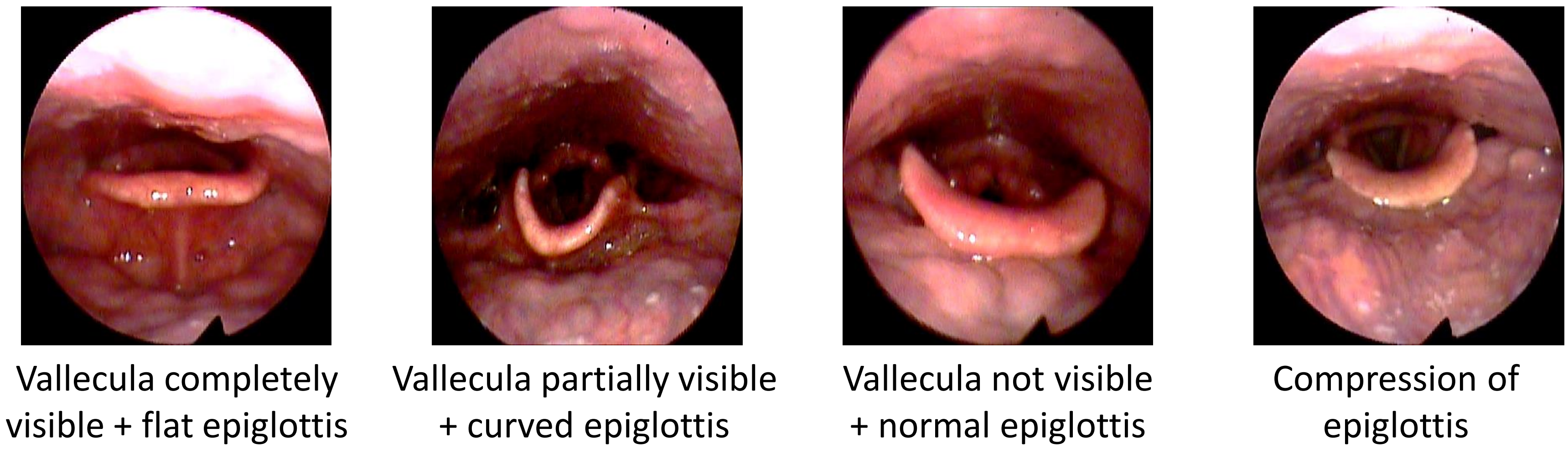
A. Soft palate



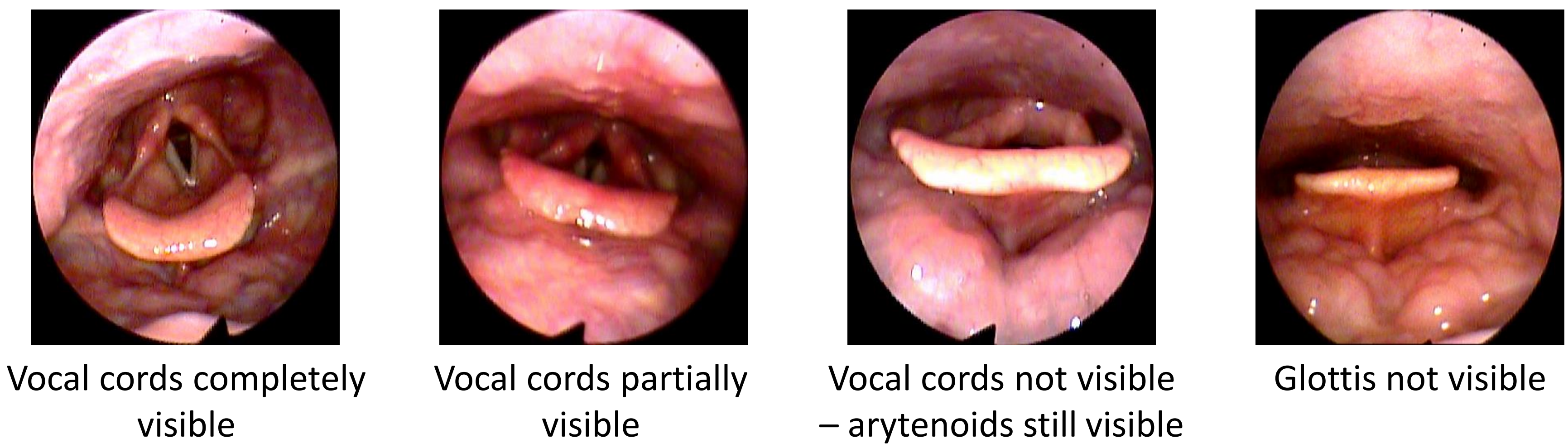
B. Oropharynx

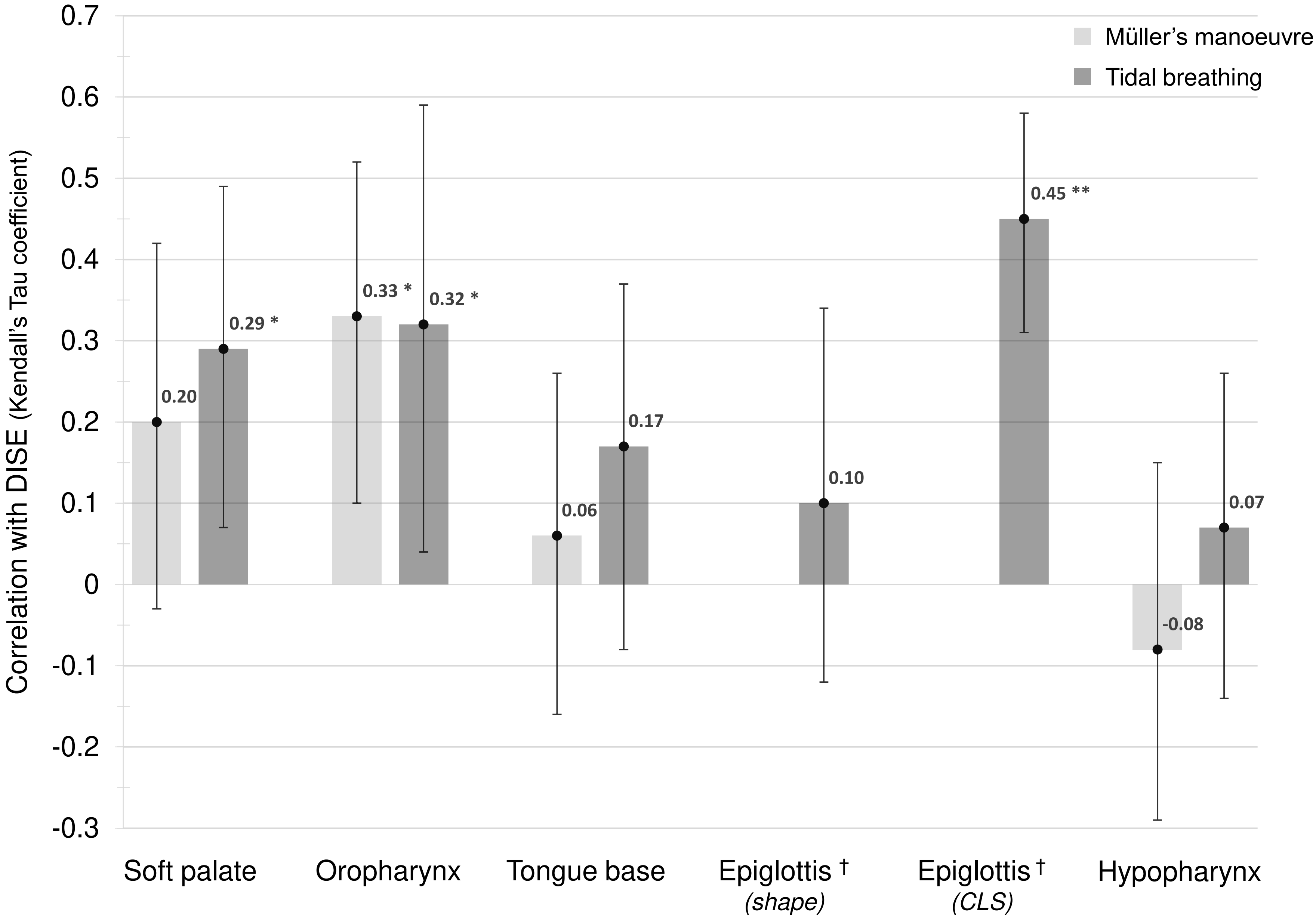


C. Tongue base + epiglottis



D. Hypopharynx (modified Cormack-Lehane scale)




0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
Correlation with DISE (Kendall's Tau coefficient)
Müller's manoeuvre
Tidal breathing
0.20
0.29 *
0.33 *
0.32 *
0.06
0.17
0.10
0.45 **
-0.08
0.07
Soft palate
Oropharynx
Tongue base
Epiglottis †
(shape)
Epiglottis †
(CLS)
Hypopharynx