Flow-Identified Site of Collapse During Drug-Induced Sleep Endoscopy

Feasibility and Preliminary Results

To the Editor:

The sites and patterns of upper airway (UA) collapse are a major outcome determinant of non-CPAP treatment in patients with OSA.[1,2] Endoscopy-based methods during sleep (natural and drug induced) are the standard approach for assessing the site(s) of UA collapse. However, these methods are invasive and require specialized equipment and personnel, limiting their generalizability.

Flow shape analysis is an emerging method to noninvasively estimate UA collapse sites. Negative effort dependence (NED), defined as the percent reduction in inspiratory flow from peak to plateau, is a cardinal flow limitation feature. It characterizes a decrease in flow despite an increase in respiratory effort. Epiglottic collapse produces a sudden drop (ie, discontinuity) in inspiratory airflow (associated with high NED)[3,4]; palatal and lateral wall collapse generate a "scooped" inspiratory flow pattern (associated with moderate NED)[4]; and tongue base collapse causes a flattened flow shape (equivalent to low NED).

Flow shape features have been successfully validated by using natural sleep endoscopy (NSE).[3-5] However, NSE is labor intensive for clinicians and challenging to undergo for patients. In contrast, drug-induced sleep endoscopy (DISE) can be performed in higher volumes during daytime hours, enabling the ability to accrue larger samples for flow shape analysis. In clinical practice, DISE is performed in the operating room without airflow or other polysomnographic signal assessments.[6] The aim of the current study therefore was to assess the feasibility of concomitant flow measurements during DISE by using a pneumotachograph and to preliminarily assess correlations between NED and UA collapse sites during DISE.

Patients and Methods

This feasibility study prospectively recruited 20 patients with an established OSA diagnosis. The study was reviewed and approved by the local ethics committee at Antwerp University Hospital and University of Antwerp (18/06/069, B300201835710). All patients provided written informed consent.

All patients underwent a standard clinical DISE with additional oximetry, EEG, electrooculography, chin electromyography, and thoracic and abdominal movement measurements. Flow was measured by using a calibrated and heated pneumotachometer (Fleisch No. 2). All signals, synchronized with endoscopic footage, were captured by using an Alice LDx6 polysomnography system (Philips Respironics). Each patient was equipped with an oronasal mask with bronchoscopy elbow connected directly to the pneumotachograph. The endoscope was inserted through the sealed elbow membrane (Fig 1).

DISE assessments were performed by an experienced ear, nose, and throat surgeon. Sedation was induced by a 1.5 mg IV bolus injection of midazolam and maintained by target-controlled infusion of propofol (started at 3.0 μg/mL and lowered based on patient reaction). To avoid excessive saliva production, 0.2 mg of glycopyrronium bromide was administered. Retropalatal and retroglossal areas were each examined for at least 7 min to ensure sufficient data in each patient at each level.

Individual flow-limited breaths were scored by one reviewer based on a standardized scoring system, specifying the level (soft palate, oropharynx, tongue base, pharyngeal lateral walls, or epiglottis), degree (none, partial, or complete), and direction (anteroposterior, circular, or lateral) of collapse.[7] Only breaths associated with nonapneic complete collapse (ie, $\geq$ 90% narrowing during a portion of but not the entire inspiratory cycle) were considered for further analysis in this preliminary dataset. Patients with $<$ 10 breaths associated with complete collapse were excluded from the analysis. Flow shape analysis on the scored flow-limited breaths was performed according to Mann et al[8] to calculate NED (NED = [maximal flow in the first 30% of inspiration − minimal flow between 25% and 75% of inspiration]/maximal flow in the first 30% of inspiration).

As a primary analysis, median NED values of patients with and without a certain collapse type were compared by using the Wilcoxon rank sum test. In this primary analysis, collapse in each subject at a particular site was classified if present more than five times during the investigation, accounting for multilevel collapse. In a secondary analysis, NED values of individual breaths were compared by using linear mixed effects modeling corrected for within-subject correlation. To ascertain the presence or absence of collapse, this secondary analysis was performed separately for breaths visualized at the retropalatal and retroglossal area. Because breaths at the retropalatal level were exclusively associated with complete palatal collapse, the secondary analysis focused on breaths at the retroglossal level (oropharynx, tongue base, pharyngeal lateral walls, or epiglottic collapse). Separate linear mixed effects models were constructed for each collapse site: NED $\sim$ site of collapse + 1|subject.

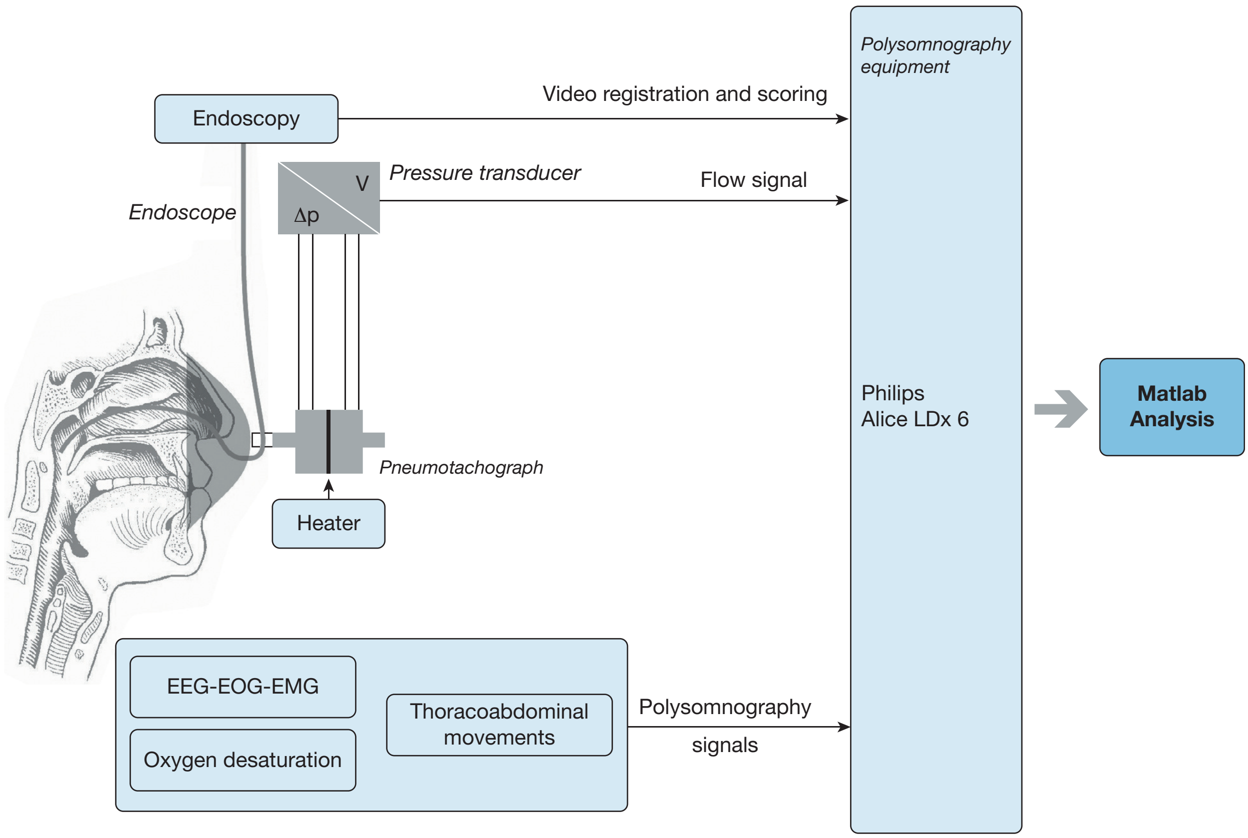

Figure 1 – *Overview of the set-up used to simultaneously measure airflow and capture drug-induced sleep endoscopy footage. The endoscope was inserted transnasally through a sealed membrane on the elbow attached to the oronasal mask. Flow was measured by using a pneumotachograph (Fleisch No. 2). Video footage, flow signals, and polysomnography signals were collected through the Philips Alice LDx6 system. EMG = electromyography; EOG = electrooculography.*

Results

Data from 17 of 20 patients were included for analysis (apnea-hypopnea index [AHI], 13.0 [11.7-14.3] events/h; supine AHI, 28.7 [17.3-40.0] events/h; BMI, 28.8 [26.3-31.3] kg/m^2; age, 65.1 [60.3-69.9] years; 59% [10 of 17] male; all, mean [95% CI]). One patient was excluded due to erroneous coupling of endoscopic footage and flow signals. Two patients had < 10 breaths associated with complete collapse. All DISE assessments were performed in < 40 min.

Primary Outcome

It was feasible to simultaneously capture airflow measurements and DISE video. In total, 1,371 breaths (81 [56-105] breaths/patient; mean [95% CI]) with complete collapse and associated flow could be obtained. Median NED values of patients with epiglottic collapse (0.60 [0.57-0.95], 5 of 17 patients, median [quartile 1-quartile 3]) were significantly higher than median NED values of patients without epiglottic collapse (0.41 [0.19-0.52], 12 of 17 patients, median [quartile 1-quartile 3]; $P = .037$).

Secondary Outcome

Individual breath-by-breath analysis was performed next, corrected for within-subject correlation. A total of 569 breaths associated with complete collapse were assessed while visualizing the retroglossal area (15 of 17 patients). Following Bonferroni correction for multiple comparisons ($P = .05/4 = .0125$), breaths with epiglottic collapse showed significantly ($P = .0120$; $\beta \pm$ SE, 0.10 $\pm$ 0.04) higher NED (0.66 [0.60-0.71], 92 breaths, 7 of 15 patients) than breaths without epiglottic collapse (0.49 [0.47-0.52], 477 breaths, 15 of 15 patients) (Fig 2). No significant differences in NED were found for the oropharynx, tongue base, or pharyngeal lateral walls.

Discussion

This feasibility study was, to the authors' best knowledge, the first study to simultaneously measure airflow and polysomnography parameters during DISE. The protocol could be fine-tuned to allow reliable pneumotachographic and polysomnographic measurements synchronized with DISE in a fast-paced setting with high patient turnover.

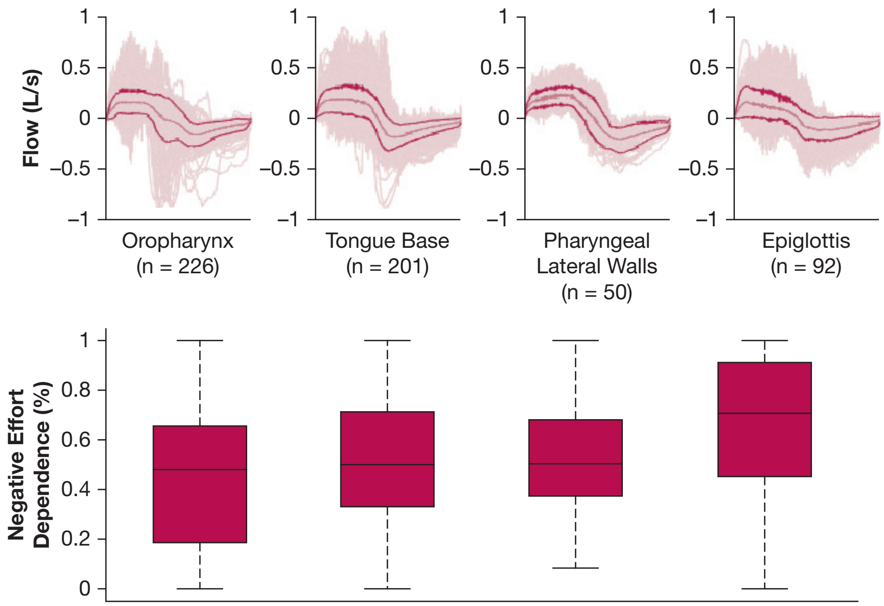

Figure 2 – *Negative effort dependence (NED) and flow traces for all breaths with complete collapse visualized at the retroglossal area (oropharyngeal, tongue base, pharyngeal lateral walls, and epiglottic collapse). Upper: median (pink trace) and interquartile ranges (dark pink) of individual breaths (light pink) associated with the different collapse sites visible at the retroglossal area. Lower: boxplots showing NED for breaths associated with the different collapse sites. Breaths with complete (> 90%) epiglottic collapse were associated with a significantly higher NED compared with breaths associated with one of the other three collapse sites visualized at the retroglossal area, as reflected in the higher flow peak during inspiration.*

Furthermore, it was possible to calculate NED from unscored polysomnographic data captured by the Alice LDx6 system.[8]

The main finding of this preliminary dataset is that patients with epiglottic collapse had significantly higher NED values than patients without epiglottic collapse. Furthermore, on a breath-by-breath level, breaths with epiglottic collapse produced significantly higher NED than breaths with complete oropharyngeal, tongue base, or pharyngeal lateral wall collapse. These findings are highly relevant because epiglottic collapse during DISE is associated with negative response to UA surgery, mandibular advancement device treatment, and CPAP.[9] Our findings confirm the results obtained with NSE showing that inspiratory discontinuity, quantified as high NED, characterizes epiglottic collapse.[4,10]

The distinction between tongue base and other collapse types shown with NSE[4] was absent in the current dataset. It is important to note, however, the difference in tongue base collapse scoring between the NSE studies and the current DISE study. Tongue-related obstruction during NSE is defined as UA crowding due to a fixed posteriorly located tongue base (thereby omitting any collapse secondary to upstream palatal collapse), whereas tongue base collapse during DISE is defined in analogy to other collapse types (ie, showing a more phasic pattern).

The current study has several potential limitations. First, the reproducibility of our findings may be limited because all endoscopic observations were made by one reviewer. Second, a wide distribution of NED was observed for every collapse site, reducing the overall accuracy to predict epiglottic collapse during DISE. This variability might be due to the limited sample size. Third, the DISE procedure, including drug administration and endoscope insertion, might have influenced the flow pattern. Previous research showed no difference in NED or UA collapsibility with and without a pharyngeal catheter.[4,11] Nevertheless, the endoscope diameter is larger, potentially increasing its impact. Furthermore, the agents used to induce sleep and reduce saliva production might have influenced collapse site and severity.[12] However, research has shown an acceptable concordance between DISE and NSE findings.[13,14] Furthermore, because clinical decision-making is often based on DISE findings, prediction of DISE collapse patterns is specifically of great interest. Fourth, our results might be influenced by the analytical approach. Because most patients with OSA experience multilevel collapse,[15] overall median NED values might be biased by different collapse levels. However, the authors argue that this approach allows for a clinically more relevant result considering patient assessment and future therapeutic response prediction. This potential limitation was partially tackled by the secondary individual breath-by-breath analysis in which the primary collapse site was detected and analyzed for each individual breath. However, due to the inherent limitation of endoscopy, not all collapse sites could be visualized simultaneously. To ascertain presence or absence of collapse, this analysis was only performed for data captured at the retroglossal level.

Because this method was not able to assess breaths captured at the retropalatal level, future research, including breaths without or with partial palatal collapse, is needed to allow comparisons between different types of palatal collapse. Finally, another limitation is the overall low (mean, 13.0 events/h) AHI. However, because DISE was uniquely performed in the supine position, the supine AHI (mean, 28.7 events/h) is presumably most relevant. Future, large prospective studies are needed using this set-up to confirm the current findings. These studies should also focus on other airflow features previously associated with UA collapse sites.[3,10]

Conclusions

This study showed the feasibility and potential of concomitant flow measurements during DISE. Our results confirmed the presence of elevated NED in epiglottic collapse.[3] This novel methodology holds promise for generating large datasets from which to develop new flow shape features. These preliminary findings also emphasize the need for comparative research in flow shape analysis between DISE and NSE.

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