A tailor made approach to obstructive sleep apnea
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Surgery for Obstructive Sleep Apnea: Sleep Endoscopy Determinants for Outcome.

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ABSTRACT

OBJECTIVES/HYPOTHESIS:

Although drug-induced sleep endoscopy is often employed to determine the site of obstruction in patients with obstructive sleep apnea (OSA) who will undergo upper airway surgery, it remains unknown whether its findings are associated with surgical outcome. This study tested the hypothesis that drug-induced sleep endoscopy variables can predict the outcome of upper airway surgery in OSA patients.

STUDY DESIGN:

Case series retrospective analysis.

METHODS:

Forty-nine OSA patients (41 male; mean apnea hypopnea index [AHI] $30.9 \pm 18.5$ events/hour) underwent propofol-induced sleep endoscopy followed by upper airway surgery (palatal surgery, and/or radiofrequency ablation of the tongue base, and/or hyoid suspension) and subsequently a follow-up polysomnography to assess surgical outcome.

RESULTS:

Twenty-three patients (47%) were responders, and twenty-nine were non-responders (53%). Non-responders had a higher occurrence of complete or partial circumferential collapse at velum and complete anteroposterior collapse at tongue base or epiglottis in comparison with responders. Multivariate logistic regression analysis revealed that among baseline clinical and polysomnographic characteristics (e.g., AHI, body mass index) and sleep endoscopy findings, the presence of complete circumferential collapse at velum, and of complete anteroposterior collapse at tongue base were the only independent predictors of upper airway surgery failure.

CONCLUSIONS:

Drug-induced sleep endoscopy can be used to predict higher likelihood of response to upper airway surgery in OSA.
INTRODUCTION

Obstructive sleep apnea (OSA) is a prevalent disorder that is associated with excessive daytime sleepiness and with an increased risk for hypertension, cardiovascular and cerebrovascular incidents, and type II diabetes.\(^1\)\(^-\)\(^6\) Continuous positive airway pressure (CPAP) is often employed as the first-line treatment for OSA.\(^7\) However, long-term compliance to CPAP treatment is considered suboptimal, prompting a substantial proportion of patients with OSA to seek alternative treatment, including upper airway surgery.\(^8\),\(^9\)

Yet, the role of such procedures in the management of OSA remains controversial, with inconsistent outcomes found in the surgical literature.\(^10\) Indeed, palatal surgery, the most commonly used surgical procedure for OSA, is associated with contradicting results ranging from a significant reduction to a considerable increase of apnea hypopnea index (AHI), with non obese and mild/moderate OSA patients having the most chances of benefitting.\(^11\),\(^12\) Thus, it is not surprising that the recommendations of the American Academy of Sleep Medicine underline the lack of rigorous data evaluating upper airway surgery and emphasize the need to preoperatively determine which populations are most likely to respond to a particular procedure.\(^10\)

Drug-induced sleep endoscopy (DISE) has been used the last two decades to determine the exact site of upper airway collapse in OSA patients.\(^13\) It is intuitively obvious that by directing surgical procedures toward obstruction-specific structures, surgical outcomes will improve.\(^14\) However, data associating DISE results with the outcome of surgical procedures are sparse and inconclusive because they have fail to determine any independent predictive value of DISE features for surgical results.\(^15\)-\(^17\) A further evaluation of DISE findings in the context of a bigger sample of patients undergoing upper airway surgery for OSA might be an important step in preoperatively distinguishing responders from non-responders, thus assisting sleep physicians in deciding the optimum treatment option.
Therefore, the aim of this study was to investigate whether DISE findings could eventually predict the outcome of upper airway surgery in OSA patients. Our hypothesis was that the level (velum, oropharynx, tongue base, epiglottis), type (circumferential, anteroposterior, lateral) and severity of collapse (partial, complete) could predict the outcome of upper airway surgery. Along with endoscopic findings, we also investigated the predictive value of known polysomnographic and clinical variables (e.g., AHI, body mass index [BMI]).

**MATERIALS AND METHODS**

**STUDY SUBJECTS**

The population retrospectively assessed for this study consisted of OSA patients who underwent propofol-induced sleep endoscopy and upper airway surgery in the Department of Otolaryngology/Head and Neck Surgery of Saint Lucas Andreas Hospital (Amsterdam, the Netherlands) during 1 year (June 2010 – June 2011). Further inclusion criteria were: 1) AHI at baseline polysomnography > 10 events/hour, 2) follow-up polysomnography at least 3 months after upper airway surgery, 3) no treatment of OSA with CPAP during the course of the followup, and 4) no upper airway surgery for OSA in the patients’ history. Patients with a history of tonsillectomy for an indication other than OSA were included. The protocol was approved by the hospital human ethics committee.

**POLYSOMNOGRAPHY**

All patients underwent a full-night diagnostic standard polysomnography before and at least 3 months postoperatively (EMBLA Titanium; Medcare Flaga, Reykjavik, Iceland). To determine the stages of sleep an electroencephalogram (C4-A1, C3-A2, O2-A1, O1-A2), electro-oculogram, and electromyogram of the submentalis muscle were obtained. Arterial blood oxyhemoglobin was recorded with the use of a finger pulse oximeter. Thoracoabdominal excursions were measured qualitatively by respiratory movement sensors placed over the rib cage and abdomen. Snoring was detected with a vibration snore sensor and body posture with a body position sensor. Airflow was monitored using
an oral thermistor placed in front of the mouth and a nasal cannula/pressure transducer inserted in the opening of the nostrils. All variables were recorded with a digital acquisition system (Somnologica 3.3; Medcare Flaga). Sleep stage was scored manually in 30-second epochs, and obstructive respiratory events were scored using standard criteria. 

**DISE**

All patients underwent DISE in supine position in the operation theatre. A topical vasoconstrictor/anesthetic combination (oxymetazoline/lidocaine) was applied to both nostrils. Propofol was administered by the anesthetist as the sole agent to achieve a target level of anesthesia of arousal to loud verbal stimulation, as per the authors’ usual protocol. 

In brief, initial infusion rate of propofol was 50 to 75 lg/kg/min, and the rate was adjusted to meet the target level of anesthesia. When achieved, a flexible endoscope was introduced into the nasal cavity. The nasal passage, nasopharynx, velum, oropharynx, tongue base, epiglottis, and larynx were observed, and the level of obstruction during inspiration was assessed.

**VOTE CLASSIFICATION**

DISE findings were illustrated using the VOTE classification system, reported previously. Accordingly, three parameters were reported: 1) site of obstruction (velum, oropharynx, tongue base, and/or epiglottis), 2) degree of obstruction (0% to 50% of narrowing corresponds to none/mild obstruction, 50% to 75% of narrowing corresponds to partial obstruction, 75% to 100% of narrowing corresponds to complete obstruction), and 3) configuration of obstruction (anteroposterior, circumferential, or lateral).

**UPPER AIRWAY SURGERY AND SUCCESS DEFINITION**

All patients underwent upper airway surgery for OSA, which included one or a combination of the following procedures: uvulopalatopharyngoplasty, Z-palatopharyngoplasty, radiofrequency ablation of the tongue base, and hyoid suspension. Multilevel surgery was considered the combination
of palatal surgery with radiofrequency ablation of the tongue base and hyoid suspension.\textsuperscript{20}

Upper airway surgery success was defined as a postoperative AHI of $< 10$ events/hour along with at least 50% decrease from the baseline AHI (responders); treatment failure was defined as a postoperative AHI of $> 10$ events/hour and/or a decrease of AHI from baseline less than 50% (non-responders).\textsuperscript{21} The postoperative difference of AHI was defined as the postoperative AHI minus the baseline AHI.

**STATISTICAL ANALYSIS**

Quantitative data are reported as mean ± SD. The normality of the data distributions was assessed by the Kolmogorov-Smirnov test. Differences in means of quantitative variables between responders and non-responders to surgical treatment were assessed by unpaired $t$ test, whereas differences in categorical values were assessed by the Yates corrected $\chi^2$ or Fisher exact test when appropriate. Multivariate logistic regression analysis followed to identify the variables that were independently associated with the response to upper airway surgery. The stepwise procedure was used to select the best logistic regression model, and the goodness of fit of this model was assessed using the Hosmer–Lemeshow test. The independent variables included in the model were those that showed significant difference in the univariate comparison between responders and non-responders to upper airway surgery; age, gender, BMI, and AHI were also included in the model despite lack of significance because of their potential importance.\textsuperscript{11, 12} A $p$-value of $< .05$ was considered to indicate statistical significance.

**RESULTS**

Among 80 patients who underwent upper airway surgery for sleep-disordered breathing between June 2010 and June 2011, 31 did not meet the inclusion criteria (10 had AHI $\leq 10$ events/hour, six patients had undergone DISE with midazolam as the sedating agent, six patients had undergone previous sleep surgery, seven patients did not have a follow-up polysomnography, and two patients used CPAP during the course of
follow-up). Of the 49 patients who met the inclusion criteria and were finally included in the analysis, eight patients underwent palatal surgery, 17 patients underwent palatal surgery with radiofrequency ablation of the tongue base, 21 underwent multilevel surgery, and three patients underwent hyoid suspension with radiofrequency ablation of the tongue base. The type of operation was decided on the basis of the level of obstruction, so that whenever palatal and/or oropharyngeal obstruction were found, palatal surgery was employed (Z-palatopharyngoplasties or uvulopalatopharyngoplasties, if tonsils have been removed or not, respectively), and whenever tongue base and/or epiglottis obstruction were found, radiofrequency ablation of the tongue base and/or hyoid suspension were employed. Patients were stratified in responders (23 patients, 47%) and non-responders (26 patients, 53%) according to follow-up polysomnography, which took place 4.1 ± 0.7 months after upper airway surgery. The postoperative difference of AHI was 26.0 ± 19.4 events/hour and -1.8 ± 14.8 events/hour in responders and non-responders, respectively. The baseline clinical and polysomnographic characteristics and the types of surgical procedures performed in these two groups of patients are summarized in Tables 1 and 2, respectively. No difference in any parameter was detected between the two groups.

Multivariate logistic regression analysis was performed to identify the independent predictors of the response to upper airway surgery. The parameters that showed significant difference in the univariate comparison between responders and non-responders (Table 3) were entered into a forward stepwise model. Additionally, age, gender, BMI, and AHI were included in the model. This analysis revealed that the independent predictors of failure to upper airway surgery were the presence of complete circumferential collapse at velum (odds ratio [OR], 5.27; 95% confidence interval [CI], 2.20–16.71; p < .001), and of complete anteroposterior collapse at tongue base (OR, 2.44; 95% CI, 1.31–5.87; p = .004). The Hosmer-Lemeshow test indicated that the fit of the model was good (p = .63). Backward procedure gave identical results.
Table 1: Anthropometric data, and clinical and polysomnographic variables in responders and non-responders.

<table>
<thead>
<tr>
<th></th>
<th>Responders (n = 23)</th>
<th>Non-responders (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>48.6 ± 10.5</td>
<td>46.0 ± 10.7</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>78</td>
<td>88</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.3 ± 3.4</td>
<td>28.7 ± 3.3</td>
</tr>
<tr>
<td>Apnoea-hypopnoea index, events/hour</td>
<td>31.9 ± 21.1</td>
<td>30.0 ± 16.1</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale score</td>
<td>8.5 ± 4.8</td>
<td>7.6 ± 5.8</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>41.0 ± 3.4</td>
<td>40.9 ± 3.3</td>
</tr>
<tr>
<td>Minimum oxygen desaturation, %</td>
<td>81.3 ± 7.9</td>
<td>82.6 ± 3.9</td>
</tr>
<tr>
<td>Tonsils size</td>
<td>1.25 ± 1.02</td>
<td>1.50 ± 0.88</td>
</tr>
<tr>
<td>Friedman score palate</td>
<td>1.85 ± 0.97</td>
<td>1.58 ± 1.00</td>
</tr>
</tbody>
</table>

Continuous data are presented as mean ± SD. There was no statistical difference between the variables of responders and non-responders.

Table 2: Surgical procedures performed in responders and non-responders.

<table>
<thead>
<tr>
<th>Surgical procedure</th>
<th>Responders (n = 23)</th>
<th>Non-responders (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palatal surgery, n (%)</td>
<td>22 (95.7)</td>
<td>24 (92.3)</td>
</tr>
<tr>
<td>Radiofrequency ablation of the tongue base, n (%)</td>
<td>18 (78.3)</td>
<td>23 (88.5)</td>
</tr>
<tr>
<td>Hyoid suspension, n (%)</td>
<td>11 (47.8)</td>
<td>13 (50)</td>
</tr>
</tbody>
</table>
Table 3: Drug-induced sleep endoscopy findings in responders and non-responders.

<table>
<thead>
<tr>
<th>Site of obstruction</th>
<th>Configuration of obstruction</th>
<th>Responders (n = 23)</th>
<th>Non-responders (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete collapse</td>
<td>Partial collapse</td>
<td>No/mild collapse</td>
</tr>
<tr>
<td>Velum</td>
<td>Anteroposterior, n (%)</td>
<td>16 (69.6)</td>
<td>6 (26.1)</td>
</tr>
<tr>
<td></td>
<td>Circumferential, n (%)</td>
<td>1 (4.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>Lateral, n (%)</td>
<td>3 (13.0)</td>
<td>17 (74.0)</td>
</tr>
<tr>
<td>Tongue base</td>
<td>Anteroposterior, n (%)</td>
<td>7 (30.4)</td>
<td>4 (17.4)</td>
</tr>
<tr>
<td>Epiglottis</td>
<td>Anteroposterior, n (%)</td>
<td>10 (43.4)</td>
<td>6 (26.1)</td>
</tr>
<tr>
<td></td>
<td>Lateral, n (%)</td>
<td>0 (0)</td>
<td>1 (4.3)</td>
</tr>
</tbody>
</table>

* p < .05 versus complete collapse of responders.
† p < .05 versus partial collapse of responders.
‡ p < .05 versus no/mild collapse of responders.
DISCUSSION

The main finding of this study were: 1) responders to upper airway surgery for OSA had a higher occurrence of complete or partial anteroposterior collapse at velum and of partial anteroposterior collapse at tongue base and epiglottis compared to non-responders; in contrast, non-responders had and a higher occurrence of complete or partial circumferential collapse at velum and of complete anteroposterior collapse at tongue base or epiglottis in comparison with responders; and 2) among baseline clinical and polysomnographic variables (e.g., AHI, BMI) and DISE findings, only the presence of complete circumferential collapse at velum and of complete anteroposterior collapse at tongue base were independently associated with failure of upper airway surgery in OSA patients.

Figure 1: Patterns of collapse on drug-induced sleep endoscopy during inspiration associated with response to upper airway surgery (A) Complete anteroposterior collapse at velum. (B) Partial anteroposterior collapse at tongue. (C) Partial anteroposterior collapse at epiglottis.

In OSA patients, especially mild and moderate cases, multiple treatment modalities besides CPAP might be considered. One of them is upper airway surgery, but given its inconsistent effect, it is of paramount importance to establish preoperative criteria, which could potentially distinguish responders from non-responders. To this end, DISE was initially employed to determine the site of obstruction and accordingly the corresponding surgical procedure. However, data associating DISE results with the outcome of surgical procedures are sparse and inconclusive. Two studies that included only patients undergoing uvulopalatopharyngoplasties, and very recently Soares et al, have all
failed to determine any independent predictive value of DISE features for surgical results.\textsuperscript{15-17} In particular, the latter authors (their work was published while the current manuscript was in the process of being written) compared a group of 15 non-responders with a group of 19 responders to upper airway surgery, and found that lateral oropharyngeal wall and supraglottic airway collapse was more prevalent in non-responders.\textsuperscript{17} The data of the current study make the findings of previous trials more conclusive in the same direction by providing evidence that propofol induced sleep endoscopy variables can predict the outcome of upper airway surgery, corroborating in that way the importance of using DISE in clinical practice.

The presence of circumferential collapse at velum was found to predict the occurrence of failure to upper airway surgery. This result is consonant with previous reports, which documented that concentric velar collapse is associated with an increased BMI and that increased BMI, in turn, is associated with surgical failure.\textsuperscript{15, 22} Accordingly, Iwanaga \textit{et al} found a lower improvement rate for patients with circumferential velar collapse (53.3\%) in comparison with patients with other types of obstruction (76.2\%). It is reasonable, then, to make the assumption that current palatal surgery might be ineffective in resolving a circumferential type of collapse.\textsuperscript{15}

Additionally, complete tongue base collapse proved to be a significant determinant of failure of upper airway surgery. This finding is consistent with previous studies, which report a positive association between the degree of tongue base collapsibility and OSA severity, and in conjunction with that, a positive association between OSA severity and surgical failure.\textsuperscript{12, 23, 24} Thus, it appears that surgical procedures addressing tongue base obstruction such as radiofrequency ablation (thermal damage to the tongue base creating lesions that diminish the bulk and flaccidity of the tongue base through fibrosis) and hyoid suspension (improvement of the retroglossal space by placing traction on the hyoid directly and advancing hyoid complex) have limited efficacy.\textsuperscript{9, 20} Interestingly, Kezirian performed DISE in non-responders to these procedures and found a high occurrence of residual tongue base collapse.\textsuperscript{25} In consequence, it is plausible to
suggest that tongue base collapse, especially in higher degrees, might be refractory to treat with the procedures currently applied, and novel treatment modalities such as hypoglossal nerve stimulation are herein greatly anticipated.\textsuperscript{26}

Figure 2: Patterns of collapse of drug-induced sleep endoscopy during inspiration associated with nonresponse to upper airway surgery. (A) Complete circumferential collapse at velum. (B) Complete anteroposterior collapse at tongue base. (C) Complete anteroposterior collapse at epiglottis.

Some possible weaknesses of the current study must be acknowledged and deserve consideration. As with any retrospective analysis, a limitation of our study was the inability to control the data.\textsuperscript{31} Furthermore, the patients undergoing upper airway surgery for OSA in our institution in most cases have BMI < 32 kg/m\textsuperscript{2} and AHI < 40 events/hour.\textsuperscript{11, 12} Consequently, our results cannot be safely extrapolated in the general population of OSA patients. Last, the precise relationship between natural and propofol-induced sleep remains elusive.\textsuperscript{28} It would be ideal if sleep endoscopy could be performed under natural sleep, but this challenging procedure is seldom applied.\textsuperscript{29} However, Rabelo et al have recently reported that although propofol reduced rapid eye movement sleep, it did not influence the respiratory pattern or significantly influence the occurrence of obstructive events.\textsuperscript{30}

CONCLUSION

This study highlights the significance of DISE by providing evidence that the presence of circumferential collapse at velum and of complete
collapse at tongue base are independently associated with failure of upper airway surgery in OSA patients. Further larger-scale studies are needed to confirm prospectively the performance of the aforementioned variables in predicting surgical outcome.

REFERENCES


