

SCIENTIFIC INVESTIGATIONS

Patients with epiglottic collapse showed less severe obstructive sleep apnea and good response to treatment other than continuous positive airway pressure: a case-control study of 224 patients

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Study Objectives: The purpose of this study was to analyze patients with epiglottic collapse, especially their clinical characteristics related to obstructive sleep apnea and phenotype labeling using drug-induced sleep endoscopy.

Methods: An age-sex matched case-control study was conducted to compare the clinical characteristics of patients with epiglottic collapse (Epi group) and patients without epiglottic collapse (non-Epi group). All patients underwent drug-induced sleep endoscopy January, 2015, to March, 2019, in a tertiary hospital for suspected sleep apnea symptoms. Demographic factors, underlying disease, overnight polysomnography, and their phenotype labeling using drug-induced sleep endoscopy were analyzed.

Results: There was no difference in age, sex, the prevalence of hypertension, diabetes, cerebrovascular disease, and coronary artery disease. However, the body mass index was significantly lower in patients in the Epi group ($P < .001$). Additionally, the apnea-hypopnea index was lower ($P = .001$), and the lowest oxygen saturation was significantly higher in the Epi group ($P = .042$). The phenotype labeling on drug-induced sleep endoscopy showed that the prevalence of velum concentric collapse and oropharyngeal lateral wall collapse was lower, and that of tongue-base collapse was higher in the Epi group. Multilevel obstructions were more common in the Epi group. However, the Epi group showed a good response to mandibular advancement or positional therapy.

Conclusions: Although there was no difference in the underlying characteristics and self-reported symptom scores between the groups, the patients with epiglottic collapse showed significantly lower body mass index and obstructive sleep apnea severity. Additionally, patients with epiglottic collapse were expected to respond well to oral devices or positional therapy.

Keywords: obstructive sleep apnea, epiglottis, airway obstruction, continuous positive airway pressure, occlusal splints

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Epiglottic collapse emerges as an important obstruction site in patients with obstructive sleep apnea. Recent studies have revealed that the prevalence of epiglottic collapse is higher than expected, and epiglottic collapse cannot be found in the awake state. However, little is known other than this fragmentary knowledge.

Study Impact: This study identified that patients with epiglottic collapse had different clinical characteristics compared to those of other patients with sleep apnea. The patients with epiglottic collapse had relatively low body mass index and less severe obstructive sleep apnea. Additionally, they were unlikely to respond to continuous positive airway pressure and likely to respond to other treatments, such as a mandibular advancement device, positional therapy, or surgical treatment, alone or in combination. Thus, in patients who fail continuous positive airway pressure, epiglottic collapse should be checked and the appropriate treatment considered.

INTRODUCTION

Obstructive sleep apnea (OSA) manifests in repetitive airway obstruction during sleep, resulting in apnea despite breathing efforts.¹ Airway structures such as the soft palate, tongue base, oropharynx, and epiglottis can cause airway obstruction. Patients who have sleep apnea have different types of obstructions. Some show single-site obstruction and others have multiple-site obstructions.^{2–4} In a considerable number of cases, the obstruction pattern could be different when awake or sleeping.⁴ So, drug-induced sleep endoscopy (DISE), which allows visualization of the airway during sleep using drugs, is widely performed.

One of the most significant findings of DISE was epiglottic collapse. Epiglottic collapse can be diagnosed only through DISE in OSA.^{4,5} The frequency of sleep apnea with epiglottic collapse has increased with DISE. The identification of the epiglottic collapse is critical because CPAP, the first-line therapy of OSA, may aggravate epiglottic collapse owing to its associated anatomical features.^{4,6} However, no study has evaluated the clinical characteristics of patients with epiglottic collapse. Therefore, in this study, the authors analyzed the patient clinical characteristics and phenotypes identified by DISE to eventually determine the appropriate treatment methods for epiglottic collapse.

METHODS

Patients

Patients who visited a tertiary hospital because of snoring and symptoms of sleep apnea from January, 2015, to March, 2019, were enrolled consecutively. All patients were recommended to undergo DISE. Patients with difficulty undergoing a DISE examination because of poor systemic conditions, such as pregnant women and those with a drug allergy (to propofol, for example) were excluded from the DISE examination. Those with a history of surgery in the oral cavity, oropharynx, tongue base, or larynx were also excluded.

We performed an age- and sex-matched case-control study to minimize the impact of age and sex on the study results. For this purpose, the entire group of patients who showed epiglottic collapse was designated as the case group (Epi group). Every case-patient had one matched control. There were 3 principles for matching: the same age (if not, an age difference of fewer than 3 years), the same sex, and the closest hospital visit date to that of the case-patient. The matched patients were assigned to the control group (non-Epi group).

Demographics factors, including underlying disease, height, and weight, were investigated at the initial visit. The Epworth Sleepiness Scale questionnaire was administered to determine the degree of self-reported daytime symptoms. The apnea-hypopnea index (AHI), lowest oxygen saturation during sleep, total duration with oxygen saturation levels lower than 90%, and sleep latency were checked in all patients via sleep studies. After that, DISE was performed to check the obstruction site during sleep, and the treatment effect was simulated by implementing jaw-thrust and head rotation maneuvers after a supine DISE.^{4,7} In some patients, DISE with CPAP (CPAP-DISE) was performed.

Sleep study

Overnight level-I polysomnography studies were performed using the Embla N7000 and RemLogic 2.0.0 (Natus Medical, San Carlos, CA) programs, or the NOX A1 (Nox Medical, Reykjavik, Iceland) and Noxturnal programs, according to the American Academy of Sleep Medicine guidelines.⁸ Briefly, these tests included pulse oximetry, electrocardiography, electroencephalography, bilateral electro-oculography, electromyography, an external thermistor, a nasal pressure transducer, dual thoracoabdominal respiratory inductance plethysmography belts, a microphone, and a piezoelectric sensor.⁴ Polysomnograms were interpreted according to *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*, Version 2.2.⁹ A hypopneic event was defined if the peak signal excursion dropped $\geq 30\%$ for at least 10 seconds, and there was a $\geq 3\%$ decrease in oxygen saturation. In some patients, the WatchPAT and the PAT software (zzzPAT version 1.5.44.7; Itamar Medical Ltd., Caesarea, Israel) were used for a sleep test.¹⁰ The patients with WatchPAT were evenly distributed in each group, 40 in the Epi group and 41 in the non-Epi group.

DISE protocol

DISE examinations were conducted according to a previously reported protocol.^{4,7} The examinations were performed in an operating room. Intravenous propofol and/or dexmedetomidine

were used as sedative agents.⁴ Oxygen saturation, electrocardiogram, and blood pressure were monitored. The bispectral index values pursued a sedation level of 50–70.¹¹ The examinations were performed according to a planned sequential protocol: an awake endoscopy, sedation endoscopy in the supine position, sedation endoscopy with jaw-thrusts and mouth-open maneuver, and sedation endoscopy with head rotation.^{4,7,12}

To differentiate genuine epiglottic collapse from pseudo-collapse secondary to tongue-base collapse was not easy in some cases.^{13,14} In such cases, we performed DISE with CPAP (CPAP-DISE) to avoid confusion between a genuine collapse and a secondary collapse. Epiglottic collapse was defined as a collapse of the epiglottis only, away from the tongue base. For this, we applied CPAP to the patients during DISE. The CPAP was initiated at a pressure of 4 cm H₂O. The pressure was increased by 1–2 cm H₂O and observed about 1 minute at each pressure until oxygen saturation was achieved.

Additionally, the study was limited to cases where an anteroposterior collapse existed. Patients with epiglottis lateral collapse were excluded. The scoring of the DISE was in accord with the VOTE classification for the velum, oropharynx, and tongue base.¹⁵ However, a score of 2 indicated 100% epiglottis collapse instead of 75–100% collapse according to Azarbarzin et al.¹⁴

Statistical analysis

Continuous variables, such as age, body mass index, Epworth Sleepiness Scale score, snoring visual analog scale (VAS), AHI, lowest SaO₂, sleep latency, or total duration with oxygen saturation levels lower than 90%, are summarized as means \pm standard deviation. Categorical variables such as sex, underlying disease, and phenotype labeling according to each DISE maneuver are presented as proportions. Unpaired 2-tailed *t* tests or Wilcoxon signed-rank tests were performed to compare the continuous variables between the Epi group and the non-Epi group. Chi-square and Fisher's exact tests were used to compare the categorical variables. A *P*-value of $< .05$ was regarded as significant. The statistical analyses were performed using SPSS 25 software (IBM Corp., Armonk, NY).

RESULTS

A total number of 522 patients underwent polysomnography and DISE during the study period, 122 (23.4%) patients with epiglottic collapse and 400 (76.6%) patients without epiglottic collapse. Among the 122 (23.4%) patients with epiglottic collapse, 106 (20.3%) patients showed epiglottic anteroposterior collapse, and 16 (3.1%) patients showed epiglottic lateral collapse. The patients with epiglottis lateral collapse were excluded from the study. Only the 106 patients with anteroposterior collapse were designated as the Epi group. Finally, a total of 212 patients were analyzed, 106 in the Epi group and 106 in the non-Epi group.

The baseline characteristics of each group showed no age or sex differences between the 2 groups (**Table 1**). The case and control groups were well matched. The prevalence of hypertension and diabetes, cerebrovascular diseases, and coronary artery disease was not different. However, the patients in the Epi group had significantly lower body mass indexes (BMIs) than those of the non-Epi group ($P < .001$).

Table 1—The demographic factors of the study population.

| | Non-Epi Group (n = 106) | Epi Group (n = 106) | P-Value† |
|--------------------------|----------------------------|------------------------|----------|
| Age | 45.67 ± 16.95 | 45.79 ± 17.05 | .958 |
| Sex (M/F) | 20:86 | 20:86 | 1.000 |
| HTN | 20 (18.9%) | 20 (18.9%) | 1.000 |
| DM | 7 (6.6%) | 7 (6.6%) | 1.000 |
| CVA Hx | 6 (5.7%) | 2 (1.9%) | .280 |
| CAD Hx | 6 (5.7%) | 9 (8.5%) | .594 |
| BMI (kg/m ²) | 27.03 ± 4.98 | 24.54 ± 3.22 | < .001 |

†Chi-square and Fisher's exact tests were performed to analyze sex and underlying disease. Student's *t* test was used to analyze age and BMI. BMI = body mass index, CAD Hx = coronary artery disease history, CVA Hx = cerebrovascular accident history, DM = diabetes mellitus, Epi = patient with epiglottic collapse, F = female, HTN = hypertension, M = male, non-Epi = a patient without epiglottic collapse.

Table 2—Comparison of self-reported symptoms and sleep study findings between patients without epiglottic collapse (non-Epi group) and patients with epiglottic collapse (Epi group).

| | Non-Epi Group (n = 106) | Epi Group (n = 106) | P-Value† |
|-----------------------------|----------------------------|------------------------|----------|
| Epworth Sleep Scale | 7.44 ± 4.58 | 7.77 ± 4.61 | .600 |
| Snoring VAS | 6.82 ± 2.40 | 5.75 ± 2.59 | .013 |
| AHI, events/h | 27.35 ± 25.37 | 17.24 ± 17.18 | .001 |
| Lowest SaO ₂ (%) | 81.53 ± 10.60 | 84.77 ± 11.30 | .042 |
| Sleep latency (min) | 16.47 ± 18.40 | 17.3 ± 15.49 | .734 |
| OD90 (%) | 8.11 ± 18.25 | 3.75 ± 11.51 | .059 |

†Student's *t* test was used to compare the non-Epi group and the Epi group. AHI = apnea-hypopnea index, OD90 = total duration with oxygen saturation levels lower than 90%, SaO₂ = oxygen saturation, VAS = visual analog scale.

There was no difference in the Epworth Sleepiness Scale scores ($P = .600$). However, the snoring VAS scores were lower in the Epi group ($P = .013$). Additionally, the sleep study results were less severe in the Epi group (Table 2). The AHI was significantly lower ($P = .001$), and the lowest saturation was significantly higher in the Epi group ($P = .042$). The AHI is known to be associated with BMI.¹⁶ Thus, we analyzed whether the BMI of the Epi group was lower after adjusting for the AHI. The binary logistic regression model showed that BMI ($P < .001$, odds ratio [OR] = 0.843) and the AHI ($P = .002$, OR = 0.970) were significantly lower in the Epi group after adjusting for the other variable (BMI or AHI).

The phenotype labeling on DISE showed some differences between the groups. All patients in the Epi group had at least one obstruction site, because the Epi group had at least epiglottic collapse in their DISE examination (Table 3). Twenty-four (22.6%) of the 106 patients in the Epi group showed isolated epiglottic collapse (Figure 1). Eighty-two patients (77.4%) in the Epi group had multilevel obstructions, including epiglottic collapse. Multilevel obstruction including the epiglottis was more common in the Epi group ($P < .001$). However, when the collapse of the epiglottis was excluded, there was no difference in multilevel obstructions between the groups ($P = .316$).

The prevalence of complete anteroposterior or lateral collapse in the velum region was not different. However, a complete concentric collapse in the velum region or lateral collapse

in the oropharyngeal region was significantly lower in the Epi group ($P = .003$ and $P = .007$, respectively). The prevalence of anteroposterior collapse in the tongue base region was higher in the Epi group ($P = .045$).

Several maneuvers were implemented to predict the therapeutic effects of an oral appliance and positional sleep in patients with epiglottic collapse (Table 4).^{4,17–19} When the jaw-thrust was performed to compare the effectiveness of oral devices,¹⁷ all obstructed regions in the airway, including the velum, oropharynx, tongue base, and epiglottis, were resolved in 63 patients (59.4%).¹⁷ When the head rotation was performed to predict the effectiveness of lateral position sleep,^{18,19} 36 patients (40.0%) showed a resolution of all airway obstructions. There was no difference according to the direction of the head rotation. When confined only to the epiglottis region, epiglottic collapse was resolved in 98 (92.5%) of 106 patients by the jaw-thrust, and 76 (71.7%) and 77 (72.6%) of 106 patients were resolved by head rotation to the right side and left side, respectively. Epiglottic collapse responded better than the other sites to the simulated treatments (Figure 2).

DISCUSSION

In this study, we performed a case-control analysis of patients with and without epiglottic collapse. The clinical characteristics

Table 3—Obstruction level of the study population on drug-induced sleep endoscopy.

| | Non-Epi Group (n = 106) | Epi Group (n = 106) | P-Value† |
|---|----------------------------|------------------------|----------|
| Patients with airway obstruction (excluding epiglottis) | 91 (85.8%) | 82 (77.4%) | .156 |
| Multilevel obstruction (including epiglottis) | 42 (39.7%) | 82 (77.4%) | < .001 |
| Multilevel obstruction (excluding epiglottis) | 42 (39.7%) | 34 (32.1%) | .316 |
| Velum | | | |
| Total | 84 (82.1%) | 71 (67.0%) | .018 |
| AP | 31 (31.1%) | 39 (39.6%) | .250 |
| Lat | 4 (4.7%) | 5 (4.7%) | 1.000 |
| Concentric | 49 (46.2%) | 27 (25.5%) | .003 |
| Oropharynx (lat) | 31 (29.2%) | 14 (13.2%) | .007 |
| Tongue base (AP) | 22 (20.8%) | 36 (34.0%) | .045 |
| Epiglottis (AP) | 0 (0%) | 106 (100%) | < .001 |

Only patients with complete obstruction (VOTE classification score 2) were counted. †Chi-square and Fisher's exact test were used to compare the non-Epi group and the Epi group. AP = collapse anteroposteriorly, Epi = patient group with epiglottic collapse, lat = collapse laterally, non-Epi = patient group without epiglottic collapse.

and adequate treatment methods of the patients with epiglottic collapse were identified. The study results showed that the Epi group had a similar degree of symptoms as the non-Epi group. However, the Epi group had relatively low BMIs (Table 1) and less severe OSA (Table 2). Judging from the results of the DISE with multiple maneuvers, an oral device or positional sleep would be effective for epiglottic collapse.

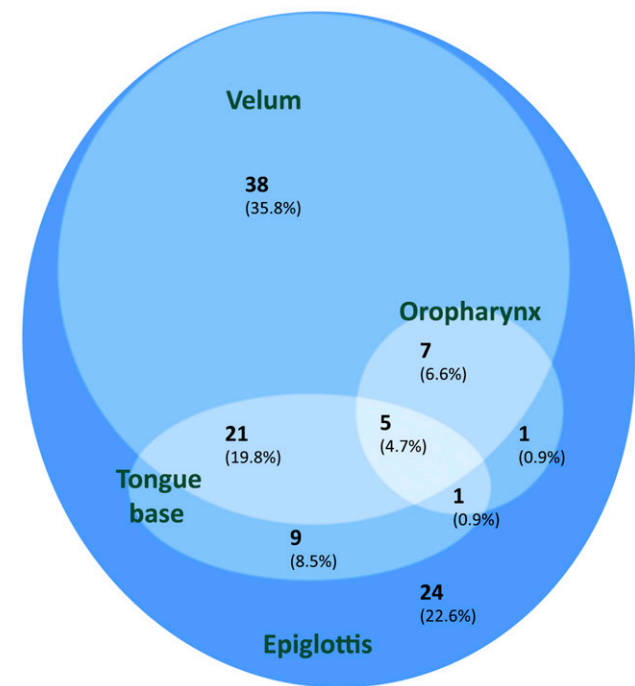
Drug-induced sleep endoscopy and epiglottic collapse

The interest in DISE is increasing. DISE can be used to identify the sites of airway obstruction. Specifically, it has strength in identifying epiglottic collapse. Epiglottic collapse is not easy to predict without sedation. So, with the advent of the DISE era, the prevalence of epiglottic collapse has increased.^{4,5,14,20} The prevalence of epiglottic collapse was reported to be 15% to 70% in a previous study population.⁵ The present study identified epiglottic anteroposterior collapse in 20.3% of the study population, and epiglottic lateral collapse in 3.1%.

Additionally, DISE can be used to predict the effects of various treatment methods by implementing several maneuvers in DISE.¹¹ The mandibular advancement device (MAD), positional sleep, and CPAP therapy can be simulated during DISE.⁴ The MAD can be simulated by the jaw-thrust and mouth-open maneuvers.¹⁷ Lateral sleep can be mimicked by the head rotation maneuver.¹⁸ CPAP can be applied and evaluated during the CPAP-DISE.^{4,21} These maneuvers facilitate identifying more efficient therapies for patients with OSA. DISE could be a tool for precision medicine in the treatment of OSA.

Also, interest in epiglottic collapse is increasing because epiglottic collapse may be a barrier to CPAP adherence, a widely used primary treatment for OSA.^{4,21-23} The anatomical shape of the epiglottis is opposite the CPAP flow.⁶ Thus, CPAP would aggravate epiglottic collapse. However, probably because of the high barrier for entry into DISE and low incidence of epiglottic collapse without DISE, a comprehensive study of epiglottic collapse is rare.

Figure 1—Obstruction sites in the epiglottic collapse patient group.



Only 24 patients (22.6%) showed isolated epiglottic collapse.

Clinical characteristics of the patients with epiglottic collapse

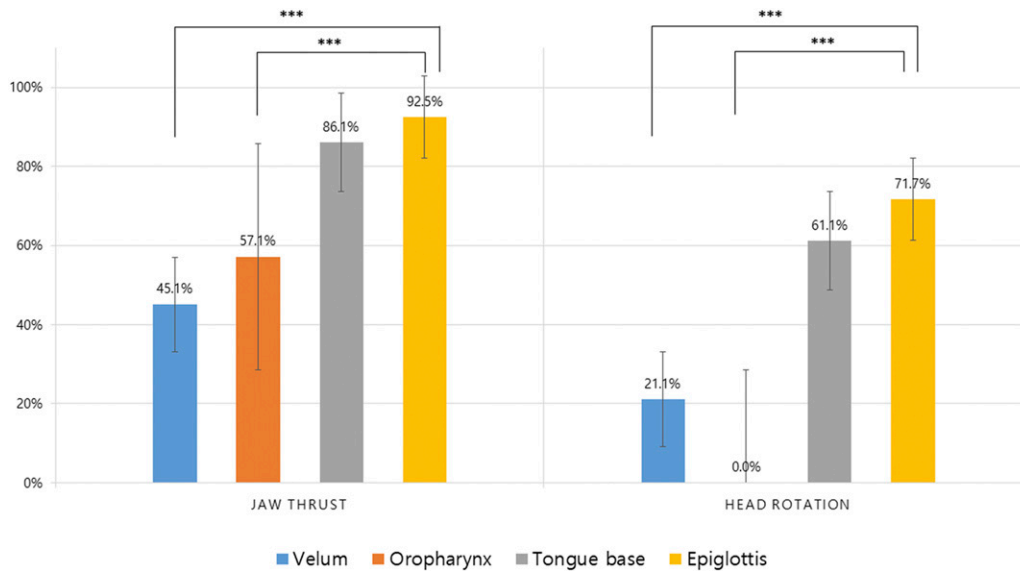
The study results showed that the prevalence of underlying disease and the severity of self-reported symptom scores had little to do with epiglottic collapse (Table 1 and Table 2). However, the BMIs were significantly lower in the patients with epiglottic collapse (Table 1). Additionally, the severity of OSA was less severe in patients with epiglottic collapse.

Table 4—Overall response of each group to the simulated treatments.

| | Non-Epi Group (n = 106) | Epi Group (n = 106) | P-Value† |
|---------------------------|----------------------------|------------------------|----------|
| Response to jaw-thrust | 51 (48.1%) | 63 (59.4%) | .130 |
| Response to head rotation | 31 (29.2%) | 46 (43.4%) | .045 |

†Chi-square and Fisher's exact tests were used to compare obstruction in the supine position and obstruction after the maneuvers.

Figure 2—The response to simulated treatments according to anatomic sites.



Epiglottic collapse responded to simulated treatments better than other obstruction sites such as the velum and oropharynx.

Phenotype labeling on DISE also showed a similar trend. DISE revealed that the Epi group showed less common concentric collapse in the velum region, and less common lateral collapse in the oropharyngeal region (Table 3). Patients with complete concentric collapse or oropharyngeal lateral wall collapse are more likely to have higher AHIs and BMIs.^{24,25} Thus, it is reasonable that the Epi group with less common complete concentric collapse and oropharyngeal lateral wall collapse had less severe AHIs and lower BMIs.

One unusual feature observed during DISE was tongue base collapse. Tongue base collapse was more commonly found in the Epi group. It seemed to be an unmatched finding to low AHIs in the Epi group. However, a correlation between tongue base collapse and AHI was not evident. For example, Ahn et al reported that tongue volume did not correlate with AHI,²⁶ consistent with our results.

Instead of AHI severity, we focused on the shape of the epiglottis and tongue base collapse. No patient in the Epi group had an omega-shaped epiglottis. The patients with epiglottic collapse seemed to have a flat-shaped epiglottis.⁴ Delakorda et al also reported that a flat-shaped epiglottis and tongue base collapse were correlated.²⁷ We speculated that floppy epiglottis was a secondary change as a result of constant pressure from tongue base collapse. However, further study is needed to identify the precise explanation for the high prevalence of tongue base collapse in the Epi group.

The prevalence of multilevel obstructions was another contradictory finding. Multilevel obstructions were associated with increased OSA severity. This study showed that multiple-level obstructions were more common in the Epi group (Table 3). However, we should consider that the Epi group only included patients showing epiglottic collapse by definition. Thus, they had at least 1 obstruction. Excluding collapses in the epiglottis region, the prevalence of multilevel obstructions was not different between the groups (Table 3).

Treatment options for patients with epiglottic collapse

We can find clues for the appropriate treatment methods for patients with epiglottic collapse. To identify proper management options, various types of maneuvers were implemented during DISE (Table 4). More than half of the Epi group responded to the mouth-open and jaw-thrust maneuvers. We already have information that isolated epiglottic collapse is responsive to the jaw-thrust maneuver.⁴ However, this result showed that the overall airway collapse in the Epi group may have a good response to an MAD. The treatment efficacy was far better when confined to the epiglottis region. Epiglottic collapse was resolved in more than 90% of the patients by the jaw-thrust and mouth-open maneuvers (Table 4). Positional therapy also had a good effect. More than one-third of the overall airway collapses in the Epi group responded to the head rotation maneuver. When confined to the epiglottis region, more than 70%

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of epiglottic collapse cases would be expected to respond to positional therapy.

Phenotype labeling using DISE indicated that surgical treatment could be a choice for patients in the Epi group. A complete concentric collapse in the velum region is a poor prognostic factor for palate surgery and a contraindication for upper airway stimulation.^{28,29} However, the incidence of complete concentric collapse was significantly lower in the Epi group. So, if these patients fail CPAP therapy and do not have a concentric collapse in the velum region, they can be potential candidates for palate surgery or upper airway stimulation with or without partial epiglottectomy.

CPAP is not a good choice for patients with epiglottic collapse. The anatomical shape of the epiglottis is contradictory to the airflow generated by the CPAP. Increased CPAP pressure may recover the level of oxygen saturation. However, epiglottic collapse would remain (**Video 2** in the supplemental material). In those patients, the epiglottis is pulled forward along the tongue base by CPAP therapy. However, the patient still has clogging symptoms and complains about using CPAP. In those patients, a partial epiglottectomy followed by CPAP can be a solution. It was reported that partial epiglottectomy resolved the clogging symptoms and improved the residual AHI of CPAP treatment.²¹

The results of this study showed that not only the epiglottis, but also the other site of obstruction, such as velum, oropharynx, and tongue base, in the Epi group was expected to respond well to jaw-thrust and head rotation. Additionally, patients in the Epi group had fewer poor prognostic factors for surgical treatment. Thus, in patients with difficulty using CPAP, it is possible to suggest other treatments, such as a MAD, sleep position change, and surgery. However, treatment methods other than CPAP do not resolve all of the structural obstructions. There are cases where the obstruction remains. CPAP should be considered in those cases as well. Therefore, combined modality therapy, MAD, positional therapy, partial epiglottectomy, and CPAP can be considered for treating patients with epiglottic collapse.²¹

Limitations

The limitations of this study include its retrospective study design that inevitably contains inherent biases related to referral patterns and patient selection procedures. In addition, most of the patients who visit our hospital are Korean. Thus, caution should be taken in generalizing the results to other ethnicities. Third, we verified epiglottic collapse only through DISE. However, it is challenging to implement DISE in all patients suspected of epiglottic collapse. Other tools that can identify epiglottic collapse are needed. Finally, the simulated treatment outcomes were not directly assessed in these patients. Care must be taken to apply the results of this study in clinical practice.

CONCLUSIONS

The patients with epiglottic collapse had relatively low BMIs and less severe OSA. However, the symptoms of OSA were similar to those of patients without epiglottic collapse. They were unlikely to respond to CPAP monotherapy. However, the

simulated treatment results showed the possibility of applying a MAD and positional therapy to patients with epiglottic collapse. Therefore, additional evaluations such as DISE are recommended for patients who fail CPAP, and those patients should be appropriately managed.

ABBREVIATIONS

AHI, apnea-hypopnea index
 BMI, body mass index
 CPAP, continuous positive airway pressure
 DISE, drug-induced sleep endoscopy
 MAD, mandibular advancement device
 OSA, obstructive sleep apnea

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