The Laryngoscope
Lippincott Williams & Wilkins

The Efficacy of Multilevel Surgery of the Upper Airway in Adults With Obstructive Sleep Apnea/Hypopnea Syndrome

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Objective: Many patients with obstructive sleep apnea/hypopnea syndrome (OSAHS) are incapable of using continuous positive airway pressure. These patients therefore turn to surgical options as a salvage treatment. Early studies and reviews focused on the efficacy of uvulopalatopharyngoplasty, a single-level procedure for the treatment of OSAHS. Since OSAHS is usually caused by multilevel obstructions, the true focus on efficacy should be on multilevel surgical intervention. The purpose of this paper is to provide an overview of the literature on multilevel surgery for OSAHS patients.

Study Design: Systematic review of the literature and meta-analysis focusing on subjective and objective outcomes of patients with OSAHS treated with multilevel surgery of the upper airway.

Methods: We searched PubMed, the Cochrane database, and MEDLINE bibliographic databases up to March 31, 2007, for studies dealing with multilevel surgical modification of the upper airway for the treatment of OSAHS. Additional studies were identified from their reference lists. Articles were included only if the surgical intervention involved at least two of the frequently involved anatomic sites: nose, oropharynx, and hypopharynx.

Results: After applying specific inclusion criteria, 49 multilevel surgery articles (58 groups) were identified. There were 1,978 patients included in the study. The mean minimal follow-up time was 7.3 months (range, 1 to 100 months). A meta-analysis was performed to redefine the success rate to be consistent with the commonly agreed upon criteria, namely "a reduction in the apnea/hypopnea index (AHI) of 50% or more and an AHI of less than 20." "Success" implies an improved condition and is not meant to imply cure. The recalculated success rate was 66.4%. The overall complication rate was 14.6%. The evidence-base medicine (EBM) level of these 49 studies revealed that only one study was EBM level 1, two papers were EBM level 3, and the other 46 papers were ranked as level 4 evidence.

Conclusions: Multilevel surgery for OSAHS is obviously associated with improved outcomes, although this benefit is supported largely by level 4 evidence. Future research should focus on prospective and controlled studies.

Key Words: Obstructive sleep apnea, surgery, multilevel treatment, meta-analysis, effectiveness, outcomes, multilevel OSAHS surgery, OSAHS surgery review.

***Laryngoscope,* 118:902–908, 2008**

INTRODUCTION

Continuous positive airway pressure (CPAP) is the primary treatment of obstructive sleep apnea/hypopnea syndrome (OSAHS). Although studies[1,2] on CPAP compliance report results that vary from 28% to 80%, researchers agree that a certain number of OSAHS patients cannot or will not use CPAP.

Surgery for OSAHS is not a substitute for CPAP, but it is a salvage procedure for those who failed CPAP and other conservative therapies and therefore have no other options. The goal of surgical correction in the upper airway is to reduce the number and severity of obstructive events when complete elimination of these events is not possible. The term "classical cure" is used to comply with standard language of the literature but should be restated as "classical improvement" or "success." Previous studies on the efficacy of surgery for OSAHS have focused on the most commonly performed procedure, uvulopalatopharyngoplasty (UPPP).[3] This procedure only corrects obstruction of the palate and tonsils. Since it is clear that most OSAHS patients have multilevel disease including nasal and retrolingual obstructions, the appropriate surgical treatment should be multilevel. In the last decade, a significant increase in publications on multilevel approach

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Editor's Note: This Manuscript was accepted for publication December 4, 2007.

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DOI: 10.1097/MLG.0b013e31816422ea

for OSAHS patients illustrated the trend away from single-level surgery.

The purpose of this study was to systematically review all English-language published data on multilevel surgery for OSAHS patients.

MATERIALS AND METHODS

A comprehensive computer-based search of the published medical literature was performed using PubMed, the Cochrane database, and MEDLINE bibliographic database as of March 31, 2007. Search terms used included medical subject headings and the key words "sleep apnea," "surgery," "nose," "palate," "tongue," "tongue base," "hypopharynx," "hyoid," "epiglottis," "genioglossus," "radiofrequency," "advancement," "glossectomy," "suspension," and "stabilization." Article titles and abstracts were reviewed to determine article eligibility in comparison to our inclusion criteria. All relevant full-text articles were carefully studied and the lists of references were searched to identify additional pertinent reports. If the same subjects were included in separate reports, only the study with the largest and longest follow-up sample size was included, and authors were contacted for clarification when possible. Two independent authors performed duplicate assessment of data to ensure that no errors were made. The inclusion criteria were as follows:

1) The article must be written in English and study subjects must be human adults more than 18 years old.
2) The surgical treatment must be clearly described and consist of at least two target levels of obstructive sites in the nose, oropharynx, or hypopharynx.
3) The study must present sufficient pre- and postoperative data to allow calculation of subjective or objective outcomes.

Reviews, editorials, and letters were excluded from our evaluation. We also excluded studies that were suspicious of duplicating a published database or lacking appropriate baseline and postoperative data. If there were multiple follow-up PSG data in the reported results, we selected patients and data with the longest follow-up time in the study. If there were many OSAHS subgroups to compare different combinations of surgical techniques in the paper, we selected the subgroups that had a multilevel treatment and completed pre- and postoperative follow-up for this study.

All studies were reviewed for the following information:

- preoperative characteristics of the patient populations, such as age, sex, and body mass index (BMI) (kg/m^2),
- results of pre- and postoperative polysomnography (PSG) including apnea/hypopnea index (AHI), apnea index (AI), percentage of rapid eye movement stage (% REM), mean saturation of oxygen (mO_2, %) and lowest oxygen saturation (LSAT, %),
- success rate, as originally reported in the included literature,
- redefined success rate by the most common criteria (a reduction in AHI of 50% or more and an AHI of less than 20), if the raw data of individual patient was available in the paper or we contacted the authors directly,
- percentage of patients who got worse after surgery,
- subjective sleep-related breathing disorder symptoms, including bedpartner's snoring visual analogue scale (VAS, 0–10), Epworth sleepiness scale (ESS), quality of life (QOL),
- postoperative complications, and
- level of evidence.

The operative techniques included the following:

1) nose—submucosal resection of septum and inferior turbinate, endoscopic sinus surgery, polypectomy, radiofrequency (RF) turbinate surgery, and nasal valve suspension;
2) oropharynx—UPPP, tonsillectomy, transpalatal advancement pharyngoplasty, uvuloflap, uvulopalatal flap, extended uvulopalatal flap, laser-assisted uvuloplasty, RF palatal surgery and Pillar implant technique; and
3) hypopharynx—maxillomandibular advancement, midline glossectomy, mildline laser glossectomy, laser lingual tonsillectomy, genioglossus advancement, genioglossus advancement with hyoid suspension, tongue base reduction with hypoepiglottoplasty, partial epiglottidectomy, hyoid suspension to the mandible, thyrohyoid advancement, tongue base suspension with the repose system, and RF tongue reduction.

The level of evidence-based medicine (EBM) was based on the study design and the quality of the study. The study design and its corresponding level of evidence are listed on Table I.[4]

Data were analyzed using SAS 9.1 (1990, SAS Statistical Institute, Cary, NC). Meta-analytic techniques described by Rosenthal[5] were used to combine P values from different studies into a single P value that assessed overall significance. P value of less than .05 was determined statistically significant. When precise P values were not presented in the results, we computed them using either the raw data or means and standards deviations reported by the authors. The meta-analyses were weighted by the sample size in the individual studied groups. Mean percentage changes in AI and AHI are presented after excluding outliers, defined as increases in either of these measures of more than 100%.

RESULTS

In total, 79 studies on multilevel surgery for OSAHS patients were retrieved initially. After applying specific inclusion criteria, 49 multilevel surgery articles (58 groups) were identified for final inclusion.[6–54] There were 1978 subjects included in the study with a pooled mean age of 46.2 years. The mean minimal time period from multilevel surgery to postoperative PSG was 7.3 months (range, 1 to 100 months).

Success Rate of Multilevel Surgery For Obstructive Sleep Apnea/Hypopnea Syndrome

The originally reported success rate in the included literature was 64.5%. However, the definition of success used by the authors of the various papers reviewed was

TABLE I.
Summary of the Oxford Centre for Evidence-Based Medicine Levels of Evidence (May 2001).

Level	Definition
Level 1	Randomized controlled trails or a systematic review (meta-analysis) of randomized controlled trails.
Level 2	Prospective (cohort or outcomes) study with an internal control group or a systematic review of prospective, controlled trials.
Level 3	Retrospective (case-control) study with an internal control group or a systematic review of retrospective, controlled studies.
Level 4	Case series without an internal control group (retrospective reviews; uncontrolled cohort or outcome studies).
Level 5	Expert opinion without explicit critical appraisal, recommendation based on physiology/bench research, literature reviews, and animal studies.

not consistent. There were seven different definitions for success after multilevel surgery in these articles, including 1) 50% reduction in AHI and an AHI <20 events per hour; 2) a postoperative AHI reduction of at least 50% and below a value of 15; 3) a reduction of greater than 50% and an AI of less than 10 events per hour; 4) an AHI <20 events per hour, with normal O_2 saturation (≥95%) postoperatively; 5) 50% reduction in preoperative AHI; 6) a postoperative AHI <10 events per hour; and 7) a postoperative AHI reduction of at least 50% or below an AHI value of 15. Therefore, a meta-analysis was performed to redefine the success rate to be consistent with the commonly agreed upon criteria—namely "a reduction in AHI of 50% or more and an AHI of less than 20."[55] The recalculated success rate was 66.4%. Excluding eight groups with maxillomandibular advancement, the originally reported success rate in this review was 57.8% and the redefined success rate was 59.2%.

Effects of Multilevel Surgery on Subjective and Objective Data

Table II summarizes baseline and percentage change data in this review. Standard meta-analytic techniques for combining *P* values between studies after weighting for sample size found that there were significant changes in AI, AHI, % REM sleep, LSAT, snoring VAS, ESS, and QOL. The weighted average percentage change of AI showed a 55.6% improvement after multilevel surgery ($P = .035$). The weighted average percentage change of AHI showed a 60.3% improvement after multilevel surgery ($P < .0001$). An improvement in LSAT was reported in 18 of 33 groups and the weighted average percentage change showed a 10.8% improvement ($P = .028$) after multilevel surgery. ESS showed an improvement in 23 of 26 groups and the weighted average percentage change improved by 43.0% ($P < .0001$) postoperatively. Although the number of studies on the change in % REM sleep, snoring VAS, and QOL was limited, results indicated that postmultilevel surgery was associated with a 44% increase in % REM sleep (four groups, n = 329, $P < .0001$), a 65.1% decrease in bedpartner's snoring VAS (nine groups, n = 328, $P = .02$), and a 8.8% increase in QOL (three groups, n = 77, $P < .0001$). The percentage changes of weighted average on mO_2 and BMI revealed no significant difference after surgery.

Severity of Disease: Impact on Results

We also analyzed the efficacy of multilevel surgery in OSAHS patients with different disease severity, mild/moderate disease (preoperative AHI less than 40) versus severe disease (preoperative AHI greater than 40.). The originally reported success rate in the included literature was 56.1% for mild/moderate disease and 67.6% in the groups with severe disease. The recalculated success rates with a meta-analysis using the commonly agreed upon criteria (postoperative AHI of 50% or more and an AHI of less than 20)[55] were 56.5% for mild/moderate disease and 69.3% for severe disease, respectively.

Table III summarizes baseline and percentage change data for the patients with mild/moderate disease. Standard meta-analytic techniques for combining *P* values between studies after weighting for sample size found significant changes in AHI, ESS, and QOL. Table IV summarizes baseline and percentage change data for patients with severe disease. Standard meta-analytic techniques for combining *P* values between studies after weighting for sample size found that the significant changes in AHI, % REM sleep, LSAT, snoring VAS, and ESS.

Postoperative AHI increased in 9.8% of the patients overall (13.2% in those with mild/moderate disease and 6.9% in those with severe disease). The complication rate for multilevel treatment basically is the sum of the complications for each of the individual procedures. The overall complication rate is 14.6% in this review and 16% in those with mild/moderate disease and 14.2% in those with severe disease.

TABLE II.
Mean Data for Multilevel Surgery in OSAHS Patients (58 Groups, n = 1,978).

	Baseline Values				Percentage Change				
Variable	Weighted Average	Range	Number of Groups	Total n	Weighted Average %	Range %	Number of Groups	Total n	*P*
Age (years)	46.2	35.8 to 56.0	41	1,120	—	—	—	—	—
AI (/hour)	17.3	5.0 to 48.9	17	510	−55.6	−91.7 to −27.0	16	498	.035
AHI (/hour)	48.0	12.9 to 76.2	57	1,962	−60.3	−94.5 to 11.7	54	1,933	<.0001
REM sleep (%)	12.2	8.6 to 16.0	4	329	44.0	23.8 to 48.7	4	329	<.0001
LSAT	75.6	63.5 to 86.3	33	1,376	10.8	−1.85 to 36.3	31	1189	.028
mO_2	91.4	77.0 to 93.2	7	213	1.9	0.3 to 17.8	7	213	.655
Snoring VAS	8.1	7.5 to 9.3	9	328	−65.1	−72.4 to −34.7	9	328	.020
ESS	12.9	7.4 to 18.2	26	806	−43.0	−73.7 to −17.6	26	806	<.0001
QOL	16.3	15.6 to 16.9	3	77	8.8	7.1 to 11.5	3	77	<.0001
Body mass index (kg/m^2)	29.5	25.9 to 36.0	39	1,343	−1.3	−8.1 to 7.6	25	922	.309

n = number; OSAHS = obstructive sleep apnea/hypopnea syndrome; AI = apnea index; AHI = apnea/hypopnea index; REM = rapid eye movement stage; mO_2 = mean saturation of oxygen; LSAT = lowest oxygen saturation; VAS = visual analogue scale; ESS = Epworth sleepiness scale; QOL = quality of life.

TABLE III.
Mean Data for Multilevel Surgery in OSAHS Patients With AHI Less Than 40 (21 Groups, n = 588).

	Baseline Values				Percentage Change				
Variable	Weighted Average	Range	Number of Groups	Total n	Weighted Average %	Range %	Number of Groups	Total n	*P*
Age (years)	47.9	40.2 to 56.0	14	359	—	—	—	—	—
AI (/hr)	11.3	5.0 to 18.9	7	162	−55.4	−76.4 to −37.2	7	162	.317
AHI (/hr)	32.5	12.9 to 38.9	21	588	−44.4	−70.9 to 3.0	20	580	.039
REM sleep (%)	15.0	15.0 to 15.0	1	15	23.8	23.8 to 23.8	1	15	—
LSAT	80.9	72.7 to 86.3	10	289	4.6	−1.85 to 12.7	10	289	.740
mO_2	92.2	91.4 to 93.2	6	203	1.1	0.3 to 1.4	6	203	.655
Snoring VAS	8.1	7.5 to 9.3	2	23	−38.7	−46.2 to −34.7	2	23	.566
ESS	11.1	9.1 to 14.5	12	315	−34.4	−62.4 to −17.6	12	315	.001
QOL	16.3	15.6 to 16.9	3	77	8.8	7.1 to 11.5	3	77	<.0001
Body mass index (kg/m^2)	28.4	25.9 to 34.1	15	404	−2.0	−3.2 to 0	9	246	.996

n = number; OSAHS = obstructive sleep apnea/hypopnea syndrome; AI = apnea index; AHI = apnea/hypopnea index; REM = rapid eye movement stage; mO_2 = mean saturation of oxygen; LSAT = lowest oxygen saturation; VAS = visual analogue scale; ESS = Epworth sleepiness scale; QOL = quality of life.

The EBM level of this 49 papers revealed that only one paper[29] was level 1, two papers[31,50] were level 3, and the other 46 papers were ranked as level-4 evidence.

DISCUSSION

Fujita[3] first described different anatomic levels of obstruction in OSAHS. He recognized that half of the patients who underwent UPPP were nonresponders. Most of the nonresponders were identified as having multilevel obstruction. Combined oropharyngeal and hypopharyngeal obstruction was noted in 54.5% (36 of 66) of patients in his study. Thus, it is clear that Fujita himself never intended to suggest that UPPP will cure most patients with OSAHS. In 1993, Riley et al.[10] reported their surgical experience, outlining a multilevel concept. Each patient was classified as having single-level obstruction involving oropharynx only (type one) or the hypopharynx only (type three). Multilevel obstruction was identified as type two and implied a combination of oropharyngeal and hypopharyngeal obstruction. Of the 239 patients, 93.3% (223 patients) were identified as having multilevel obstruction, type 2. This early classification by Fujita and Riley was based on physical examination of the patients with vague guidelines. Specific criteria for identifying unilevel versus multilevel obstruction were not reported. Subsequent development of the Friedman tongue position (FTP) allowed for a simplified method of staging the levels of obstruction.[56] The early data based on FTP indicated that approximately 25% of patients presenting with OSAHS had unilevel obstruction, while 75% had multilevel obstruction. Abdullah and van Hasselt[57] confirmed the high incidence of multilevel disease and 87% of their 893 patient populations had multilevel obstruction.

TABLE IV.
Mean Data for Multilevel Surgery in OSAHS Patients With AHI Greater Than 40 (37 Groups, n = 1,390).

	Baseline Values				Percentage Change				
Variable	Weighted Average	Range	Number of Groups	Total n	Weighted Average %	Range %	Number of Groups	Total n	*P*
Age (years)	45.4	35.8 to 52.0	27	761	—	—	—	—	—
AI (/hour)	20.1	10.0 to 48.9	10	348	−55.8	−91.7 to −27.0	9	336	.059
AHI (/hour)	54.6	42.8 to 76.2	36	1374	−67.1	−94.5 to 11.7	34	1353	<.0001
REM sleep (%)	12.1	8.6 to 16.0	3	314	15.0	25.0 to 48.7	3	283	<.0001
LSAT	74.1	63.5 to 82.1	23	1087	12.8	1.3 to 36.3	21	900	.012
mO_2	77.0	77.0 to 77.0	1	10	17.8	17.8 to 17.8	1	10	—
Snoring VAS	8.1	7.6 to 9.3	7	305	−67.1	−72.4 to −58.0	7	305	.014
ESS	14.1	7.4 to 18.2	14	491	−48.5	−73.7 to −32.8	14	491	.0005
QOL	—	—	—	—	—	—	—	—	—
Body mass index (kg/m^2)	30.0	26.3 to 36.0	24	939	−1.0	−8.1 to 7.6	16	676	.109

OSAHS = obstructive sleep apnea/hypopnea syndrome; AI = apnea index; AHI = apnea/hypopnea index; REM = rapid eye movement stage; mO_2 = mean saturation of oxygen; LSAT = lowest oxygen saturation; VAS = visual analogue scale; ESS = Epworth sleepiness scale; QOL = quality of life.

Classifications of Multilevel Surgery

Published data on multilevel treatment can be divided into four groups:

1) The most commonly performed multilevel approach includes a UPPP as a basic technique with a second procedure designed to improve the hypopharyngeal airway. Most commonly this includes genioglossus advancement, thyrohyoid advancement, RF tissue volume reduction of the tongue base, and in some cases, tongue base suspension. The success rate for these procedures has been reported to be between 20% and 100%.
2) The second group of patients studied who have undergone multilevel treatment include those who have had more invasive and more radical hypopharyngeal surgery such as open tongue base resection. Because of the aggressive nature of these procedures, most of these patients had a temporary tracheotomy and required significant hospitalization. There was significant postoperative morbidity as well. The success rate in this group varied between 44% and 100%.
3) The third group of multilevel surgery for OSAHS included patients undergoing bimaxillary advancement as part of the multilevel treatment program. Most of these patients had undergone a staged surgery, often with UPPP and genioglossus advancement as their primary procedure. The success rate of this group varies from 65.2% to 97.5%.
4) The fourth group includes patients who underwent multilevel minimally invasive techniques for mild/moderate OSAHS. Steward et al.[38] studied 22 patients who underwent combined RF reduction of the palate and the base of tongue and reported a success rate of 59%. None of their patients had concomitant nasal surgery. Fischer et al.[32] presented a similar study about multilevel minimally invasive surgery with RF on the palate, tonsil, and tongue base for 15 OSAHS patients. Stuck et al.[36] published their surgical results with RF on the palate and base of the tongue for 18 OSAHS patients with mild/moderate disease. In 2007, we presented minimally invasive single-stage multilevel surgery for patients with mild/moderate OSAHS.[58] Our patients had undergone a three-level treatment that included nasal surgery, palatal stiffening by pillar implant technique, and RF volume reduction of the tongue base with a minimum follow-up of 6 months. Classical success was achieved in 54 of 122 patients (47.5%).

Success Rate of Multilevel Surgery For Patients With Obstructive Sleep Apnea/Hypopnea Syndrome

The determination of the adequacy of OSAHS treatment remains controversial. We chose the more conservative outcome criteria and recalculated the success rate with a "classical success" definition (a reduction of AHI >50% and postoperative AHI <20).[55] This was also the most common use for evaluation of surgical results in these multilevel papers. We redefined the success rate in this study and also applied the concept of "intent-to-treat" analysis to strictly validate the original data, if the original PSG data were available or after contacting the original authors. For example, Vicente[51] presented their success rate as 78% (42 surgical successes in 54 patients who completed postoperative PSG). However, there were 55 patients in their study and 1 patient did not have postoperative PSG. Thus, we redefined the success rate as 76.7% (42 of 55). In this study, the originally reported success rate in the included literature was 64.5%. The recalculated success rate with a meta-analysis using the commonly agreed on criteria (postoperative AHI of 50% or more and an AHI of less than 20) was 66.4%.

Severity of Disease

Many otolaryngologists presume that although UPPP as a single-level treatment may not cure patients with severe OSAHS, it is likely to be effective for patients with mild disease. There are, however, many studies indicating that the severity of disease is not a predictor of success with single-level surgery.[56,59] Senior et al.[60] studied a group of patients with mild OSAHS (AHI less than 15). These patients underwent UPPP and the success rate was only 40%. Friedman further studied a series of patients with mild disease and showed an overall success rate of approximately 40% as well.[56] Most patients indeed have multilevel disease and the success for the surgical treatment of mild OSAHS is not better than that for those treating severe disease. In fact, the basis of the Friedman staging system[56] is that anatomic findings are the most significant factors, rather than the severity of disease. In this review, we analyzed the efficacy of multilevel surgery in OSAHS patients with different disease severity. The recalculated success rates were 56.5% for mild/moderate disease and 69.3% for the groups with severe disease, respectively. This review supports the concept that mild disease is not easier to correct than severe disease.

Patients Who Failed With Progression of Disease After Surgery

In this study, we found that there were only 23 studies (from their reported results and raw data) that provided the rate of progression of disease postoperatively. The overall percentage of patients with a worse postoperative AHI is 9.8%, and 13.2% in the groups with preoperative mean AHI less than 40, and 6.9% in the groups with preoperative mean AHI greater than 40, respectively. Once again, the patients with severe disease seem to do better than patients with mild disease. We also found most studies reported the postoperative objective PSG parameters, however, there was a lot of literature included that did not present the subjective outcomes. This might be due to lack of standard outcome parameters in OSAHS outcome survey or variation in skill, experience, or intraoperative bias.

Short-Term Versus Long-Term Results

Most of literature on multilevel treatment of OSAHS reported short-term surgical results at 6 months or less after surgery. The success rate varied from 0% to 100%. Vicente[51] studied the long-term efficacy of UPPP and tongue-base suspension with the repose system for severe

OSASHS and reported a 78% success rate at 3 years after surgery. Neruntarat[34] performed uvulopalatal flap in conjunction with GAHM in 46 patients and followed the short-term (6 months after surgery) and long-term (at least 37 months postoperatively) outcome. The short-term and long-term success rates were 78.3% and 65.2%, respectively. Six (16.7%) patients with short-term success failed over the long term, and these patients had a significant increase in BMI. The longest follow-up result in multilevel treatment was reported by Andsberg et al.[19] using a 50% reduction in the apnea index as the definition for success. They reported on 16 patients at 1 year and 8.4 years after surgery. Their success rates were 56% and 56%, respectively. The weights of the patients remained stable during the follow-up period.

CONCLUSION

CPAP remains the first-line standard treatment for OSAHS. However, there is a certain percentage of OSAHS patients who either fail or are unwilling to pursue CPAP therapy. For these patients, surgery offers a chance to control OSAHS. Since OSAHS is usually caused by multilevel obstructions, the true focus on efficacy should be on multilevel surgical intervention. Based on this systematic review, multilevel surgery for OSAHS is obviously associated with improved outcomes. This benefit however is supported largely by level-4 evidence. Future research should conduct larger, higher level and longer-term studies to further validate the results and direct optimal surgical intervention for each OSAHS patient.

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