EDITORIAL

Upper Airway Surgery for Obstructive Sleep Apnea

Meghna P. Mansukhani, MD; Eric J. Olson, MD; Sean M. Caples, DO, MS

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway collapse, hypoxemia, and sleep disruption; is strongly associated with cardiovascular disease; and is an important cause of excessive daytime sleepiness.[1,2] In the US, the estimated prevalence in 2013 of moderate to severe sleep apnea was 10% to 17% in men and 3% to 9% in women,[3] and the most common risk factors include advancing age, obesity, and male sex.[4] Continuous positive airway pressure (CPAP) is highly effective at maintaining upper airway patency, and has been shown in randomized clinical trials to improve symptoms of OSA, such as daytime sleepiness.[5] Although CPAP is considered first-line therapy for symptomatic OSA, a substantial proportion of patients refuse or do not tolerate CPAP,[6] leaving patients and their clinicians in search of other effective treatments.

Related article page 1168

For decades, as a means to manage OSA, surgeons have modified the upper airway with procedures such as uvulopalatopharyngoplasty (UPPP), which are designed to enlarge the airway luminal area by debulking the soft tissues that form its walls. However, enthusiasm within the sleep medicine community for such procedures has been limited by an evidence base that has primarily included studies with methodological limitations that have reported low rates of benefit in managing OSA.[7] Although a few randomized clinical trials have been published,[8] including 2 small trials (with sample sizes of 65 and 42 patients) that analyzed UPPP,[9,10] the literature primarily consists of retrospective studies and single-center case series. Notwithstanding the long list of biases inherent to such studies, including nonuniform selection criteria and loss of patients to follow-up, these surgical series also raise questions about standardization of operative technique that may not translate to other centers and surgeons. In addition, in terms of procedural safety, nonsystematic studies also may be limited by inaccuracies in ascertainment of adverse events.

The study by MacKay et al[11] reported in this issue of *JAMA* should be considered a platform for a new era in clinical trials of upper airway surgery for OSA. The Sleep Apnea Multilevel Surgery (SAMS) trial was conducted at 6 sites across Australia and randomized patients with moderate to severe OSA who could not tolerate or refused conventional treatments (some oral appliances but primarily CPAP) to undergo either a standardized soft tissue upper airway surgery (n = 51) or ongoing medical management that included weight loss and other lifestyle changes (n = 51). The "multilevel" surgery designation refers to regions within the upper airway, because in most cases of OSA airway collapse is thought to occur at multiple levels. To address this, surgeons performed a tandem procedure of modified UPPP along with radiofrequency volume reduction of the tongue designed to manage and prevent collapse of the upper airway behind the palate and tongue, respectively.

Several methodological features of the rigorous SAMS trial stand out. First, in recruiting patients who previously failed standard therapy, and by using relatively simple preoperative assessments of surgical candidacy, the investigators employed a practical clinical approach to OSA management. Second, a training workshop was conducted to standardize the surgical technique among surgeons to help ensure both internal validity and generalizability of the procedure. Third, patient-centered outcomes were incorporated. The primary outcomes not only included the change in the apnea-hypopnea index (AHI; the number of apnea or hypopnea events per hour of sleep), a standard if not compulsory measure of OSA severity, but also a change in the Epworth Sleepiness Scale (ESS) score (range, 0-24), a validated measure of subjective sleepiness, with assessment of baseline-adjusted differences between the study groups at 6 months. The secondary assessments included measures of quality of life and bed partner–reported snoring intensity.

Although the optimal candidates for surgical treatments of OSA have not been universally defined or systematically studied, traditionally these procedures are best reserved for younger and leaner patients with less severe disease. However, in the report by McKay et al[11] the study population consisted of middle-aged patients (mean age, 44.6 years) with overweight or obesity (mean [SD] body mass index of 30.7 [3.9] in the surgery group and 29.5 [3.7] in the ongoing medical management group) and fairly severe OSA.

At the 6-month follow-up, both groups showed improvements in the AHI, with significantly greater improvement in the surgery group. From baseline to 6 months, the AHI declined from 47.9 to 20.8 events per hour in the surgery group vs from 45.3 to 34.5 events per hour in the medical group (baseline-adjusted between-group difference at 6 mo, −17.6 events/h [95% CI, −26.8 to −8.4]). For the other primary outcome, change in the ESS score, the surgery group also had significantly greater improvement in subjective sleepiness compared with the ongoing medical management group. From baseline to 6 months, the ESS score declined from 12.4 to 5.3 in the surgery group and from 11.1 to 10.5 in the medical management group (baseline-adjusted between-group difference at 6 mo, −6.7 [95% CI, −8.2 to −5.2]). A number of secondary outcomes, such as snoring severity, sleep-specific quality of life, and self-rated general health, also were improved in the surgery group compared with the medical management group.

However, closer inspection reveals some limitations of the surgical treatment that are noteworthy and probably important. At 6-month follow-up, 57% of patients still had moderate to severe residual sleep apnea by polysomnographic criteria, and oxygen saturation levels, although improved compared with

baseline, persistently dipped below 85% in some patients. Such findings emphasize the importance of follow-up sleep apnea testing after surgery and raise the question of the adequacy of the surgical intervention at the targeted tissues or the possibility that airway collapse occurred at other levels of the upper airway, presumably in the hypopharyngeal area.

This finding also highlights what appears to be a discordance between the 2 primary outcomes: the high residual AHI and improvement in subjective sleepiness. As to the former, a counterargument to the importance of residual AHI has been suggested by proponents of surgery who point to the "dose" of treatment that might favor a patient having a partial but all-night reduction in the AHI over a patient having difficulty tolerating CPAP, which might reduce the AHI toward zero but at the cost of partial treatment adherence (only a few hours of CPAP use per night). In terms of the latter, the study design did not permit a placebo surgical control or blinding of patients to their treatment assignment. Therefore, it is possible that the large magnitude of change in subjective sleepiness could have been influenced by placebo effect in expectant patients who were hopeful for a CPAP alternative.[12]

Among clinicians and patients, emphasis is often placed on cardiovascular disease and the effects of OSA treatment on such outcomes; CPAP has been shown in multiple randomized clinical trials to reduce blood pressure.[5] Although the SAMS investigators approached this topic with rigor, measuring 24-hour ambulatory blood pressure, there were no significant changes detected in either group. It might be theorized that incomplete treatment effect with high rates of residual OSA and persistent hypoxemia could explain such a finding, but because the study was not powered or designed to address blood pressure primarily, such reasoning would be speculative.

As for safety, there were no deaths and there were 6 serious adverse events reported in 4 patients. In 2 of the 4 patients, the events occurred after randomization but before surgery, so adverse events possibly attributable to surgery occurred in 2 of 50 patients (4%). Without other trials to benchmark, the best comparative data are from a cohort from a 2004 Veterans Administration study that reported a 1.5% incidence of serious nonfatal complications associated with UPPP.[13] Such data, uncoupled from the rigorous outcome ascertainment methods of a clinical trial, might be an underestimate and may not be as applicable with current advances in surgical techniques.

The results from the study reported by MacKay et al[11] represent a solid foundation for future investigations, although several issues deserve consideration. First, surgery was effective at preventing upper airway collapse in some patients but not in others, suggesting that selection criteria will need to be refined in future trials. Second, as in other treatment trials of OSA, women and minority populations were underrepresented, highlighting the importance of including patients from these groups in future trials. Third, because the follow-up time was only 6 months, longer-term data from this trial and future trials will be needed to test the durability of treatment effect over time. It is conceivable that with aging or weight gain, the surgical effect on soft tissue recedes. Fourth, comparative efficacy trials are needed to test this technique against other surgical procedures, particularly maxillomandibular advancement and upper airway stimulation, which have shown promise as effective treatments for OSA.[14,15]

An important segment of patients with OSA desire alternatives to CPAP and other device treatments. The data from the study by MacKay et al[11] are proof that many patients will accept invasive therapies and will be satisfied with the improvement they achieve even with residual sleep apnea. To further refine the process and enhance patient outcomes, the methodological features of the SAMS trial should be considered the standard to which the conduct of future surgical trials in OSA should be held.

ARTICLE INFORMATION

Author Affiliations: Center for Sleep Medicine, Mayo Clinic, Rochester, Minnesota (Mansukhani, Olson, Caples); Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota (Olson, Caples).

Corresponding Author: Sean M. Caples, DO, MS, Mayo Clinic, 200 First Street SW, Rochester, MN 55902 (caples.sean@mayo.edu).

Published Online: September 4, 2020. doi:10.1001/jama.2020.9332

Conflict of Interest Disclosures: Dr Mansukhani reported receiving grants from the ResMed Foundation and the Paul and Ruby Tsai and Family Fund Career Development Award at Mayo Clinic outside the submitted work. Dr Olson reported receiving royalties from UpToDate for chapters on management of obstructive sleep apnea. No other disclosures were reported.

REFERENCES

1. Javaheri S, Barbe F, Campos-Rodriguez F, et al. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. *J Am Coll Cardiol*. 2017;69(7):841-858. doi:10.1016/j.jacc.2016.11.069

2. He K, Kapur VK. Sleep-disordered breathing and excessive daytime sleepiness. *Sleep Med Clin*. 2017;12(3):369-382. doi:10.1016/j.jsmc.2017.03.010

3. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177(9):1006-1014.

4. Lyons MM, Bhatt NY, Pack AI, Magalang UJ. Global burden of sleep-disordered breathing and its implications. *Respirology*. 2020;25(7):690-702.

5. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2019;15(2):335-343. doi:10.5664/jcsm.7640

6. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med*. 2019;15(2):301-334. doi:10.5664/jcsm.7638

7. Caples SM, Rowley JA, Prinsell JR, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults. *Sleep*. 2010;33(10):1396-1407.

8. Woodson BT, Steward DL, Weaver EM, Javaheri S. A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. *Otolaryngol Head Neck Surg*. 2003;128(6):848-861.

9. Browaldh N, Bring J, Friberg D. SKUP^{3}RCT; continuous study: changes in sleepiness and quality of life after modified UPPP. *Laryngoscope*. 2016;126(6):1484-1491. doi:10.1002/lary.25642

10. Sommer UJ, Heiser C, Gahleitner C, et al. Tonsillectomy with uvulopalatopharyngoplasty in obstructive sleep apnea. *Dtsch Arztebl Int*. 2016;113(1-2):1-8. doi:10.3238/arztebl.2016.0001

11. MacKay S, Carney AS, Catcheside PG, et al. Effect of multilevel upper airway surgery vs medical management on the apnea-hypopnea index and patient-reported daytime sleepiness among patients with moderate or severe obstructive sleep apnea: the SAMS randomized clinical trial. *JAMA*. Published online September 4, 2020. doi:10.1001/jama.2020.14265

12. Probst P, Grummich K, Harnoss JC, et al. Placebo-controlled trials in surgery. *Medicine (Baltimore)*. 2016;95(17):e3516.

13. Kezirian EJ, Weaver EM, Yueh B, et al. Incidence of serious complications after uvulopalatopharyngoplasty. *Laryngoscope*. 2004;114(3):450-453.

14. Zaghi S, Holty JE, Certal V, et al. Maxillomandibular advancement for treatment of obstructive sleep apnea: a meta-analysis. *JAMA Otolaryngol Head Neck Surg*. 2016;142(1):58-66.

15. Strollo PJ Jr, Soose RJ, Maurer JT, et al. Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med*. 2014;370(2):139-149.