As Sleep Surgery Evolves, Sleep Specialists Match Patients Who Fail CPAP to Personalized Treatments

Obstructive sleep apnea is a heterogeneous disease in which patients differ in their severity, physical features, and treatment preferences. For almost two decades, otolaryngologist and sleep medicine specialist Ofer Jacobowitz, MD, PhD, FAASM, of ENT and Allergy Associates LLP in New York City, has been matching CPAP, custom oral appliances, sleep surgery, and combination treatments to his patients. "Dr J" shares his expertise with *Sleep Review*'s audience.

By Ofer Jacobowitz, MD, PhD, FAASM

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When considering sleep apnea treatment options, whether medical or surgical, all our treatments can benefit certain patients but all are imperfect. So the best treatment modality is the one that is acceptable to the patient and can benefit him or her for the long term.

Continuous positive airway pressure (CPAP) therapy is highly efficacious at lowering the apnea-hypopnea index (AHI), but adherence in the home setting is the limiting factor for effectiveness. Recently, the cardiovascular benefits of PAP have been called into question in a randomized trial[1] and a meta-analysis study[2]; the APPLES neurocognitive effects study did not show major benefit from PAP[3] and persistent sleepiness is common with PAP treatment.[4] An obvious explanation for these results is inadequate nightly use of PAP in these studies. After all, changing a person's habits is a great challenge and not always achieved, despite our best efforts.

It has been proposed that PAP AHI effectiveness needs to be adjusted as a function of hours used and obstructive sleep apnea (OSA) severity to determine its true effectiveness. This is in contrast with surgery, where adherence is "100%" but AHI effectiveness is lower. Thus, the mean disease alleviation may ultimately be quite similar for PAP and surgery.[5] On the other hand, given that surgery is invasive and carries risks, I offer

it very selectively, after careful consideration of medical options. I am able to have the majority of patients adhere to PAP by using the proper interface, addressing side effects, adjusting device

modes and settings, and, most importantly, improving nasal airflow.

I recommend a common-sense approach to the treatment of sleep apnea, in which the goals are quality of life improvement and reduction of medical risk for a chronic disease. Have a discussion with your patient about his or her goals, which may include: getting a good night's sleep; treating snoring; improving alertness, mood, or focus; and reducing medical risk. Understanding the patient's expectations in the context of sleep habits, environment, and occupation can improve treatment matching and long-term success. A full discussion of the merits and problems associated with medical and surgical treatments is key, although insurance carrier policies often stipulate that CPAP be the first treatment option. I find visual aids and models to be useful when introducing PAP, oral appliances, and surgical options.

RATIONALE FOR SLEEP SURGERY

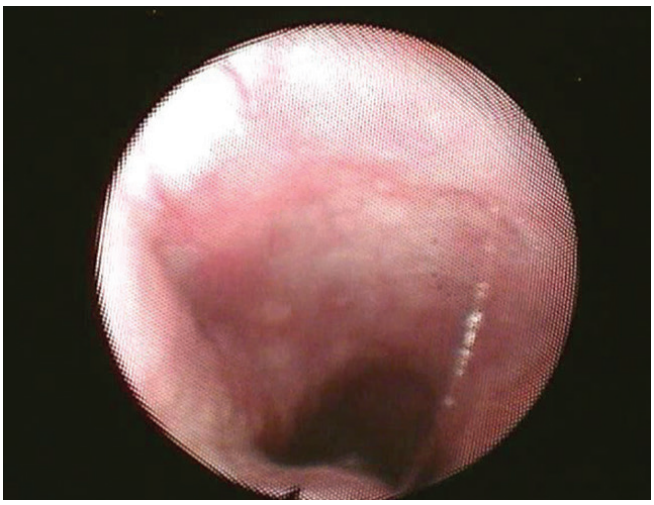
The role of sleep surgery is straightforward when we consider that the goal of treatment is to improve the patient's well-being, with the understanding that all OSA treatments are imperfect. Lowering mortality, morbidity, and improving quality of life are the key goals of any chronic disease management and also recommended in the American Academy of Sleep Medicine's Quality Measures for the Care of Adult Patients with Obstructive Sleep Apnea.[6]

In observational studies of sleep surgery, even classic uvulopalatopharyngoplasty (UPPP) has been shown to reduce mortality and cardiovascular morbidity at least as well as PAP.[7,8] Furthermore, there are high-level studies that demonstrate notable improvements in quality of life and alertness as a result of sleep surgery.[9-11]

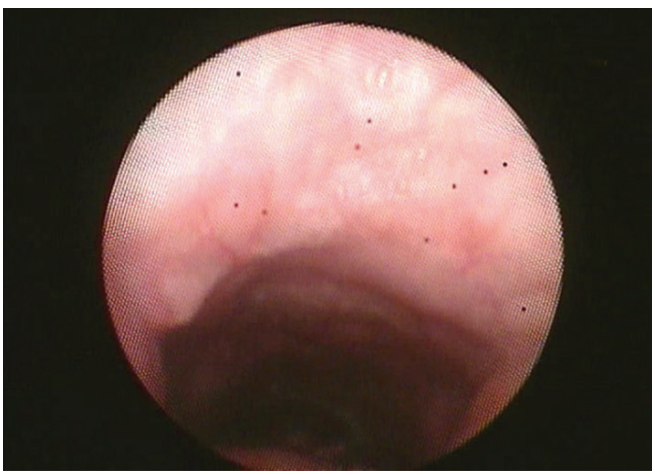
It is true that AHI is often not normalized with sleep surgery (though it is typically reduced), but this is not necessarily a problem in the real world. Patients don't come in asking, "Doctor, please reduce my AHI, but leave my snoring and sleepiness alone." AHI is not the disease but a surrogate marker for OSA and a variable target. AHI has multiple definitions; varies night to night, between centers, and across testing devices; and is not well linked with daytime sleepiness. AHI also does not normalize for some patients on PAP.[12] So surgery's "success" should not be assessed based on a single night's AHI determination, though a level <20/hour is desired for reduced mortality and morbidity risk. Since surgery is invasive and carries risk, it needs to be carefully considered, which is why I perform sleep surgery in the appropriate minority of patients.

PHARYNGOPLASTY: PAST AND PRESENT

Shortly after beginning my practice, I became interested in OSA; the sleep disorder was highly prevalent among my patients. Classic UPPP was the most common surgical procedure, but it was immediately clear to me that more was needed. UPPP was introduced in the 1980s and appeared to have great promise but unfortunately disillusionment followed, and in 1996 the procedure was labeled as "being less than 50% effective."[13] While this label was derived from a review focusing on AHI alone and not on primary outcome measures for OSA,



This image shows the pharynx of an obstructive sleep apnea patient before lateral pharyngoplasty. It was taken with a fiberoptic scope from the nasopharynx down.

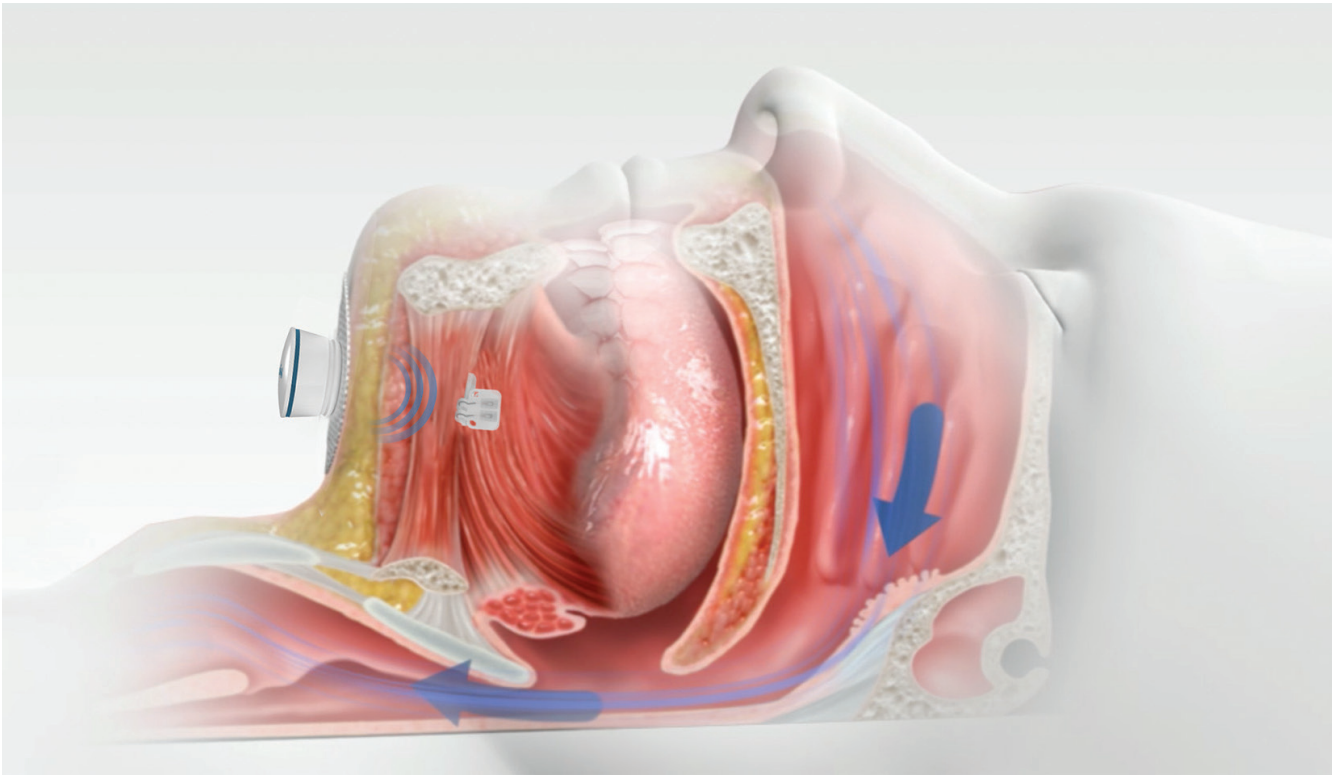


Here is the same patient post-lateral pharyngoplasty

the procedure did appear of limited value to me as it was not designed to treat the most common anatomical phenotype in my patients: lateral narrowing of the pharyngeal bottleneck. More effective procedures or combination procedures were needed.

Skeletal surgery followed, pioneered by Robert W. Riley, MD, and Nelson B. Powell, MD, who published a staged multilevel protocol. The protocol included UPPP, genioglossus advancement, hyoid suspension (phase I), and, if needed, subsequent maxillomandibular advancement (MMA, Phase II). In a study I led, Phase I multilevel surgery was effective at reducing the AHI from severe to low risk levels and improving quality of life.[14] Presumably, hyoid suspension and genioglossus advancement were providing indirect stabilization of the lateral pharyngeal walls.

MMA can effectively widen the pharynx and stabilizes the lateral pharyngeal walls. For the skeletally challenged patient, MMA can treat both OSA and cosmesis, as long as the patient



Currently in early testing, Nyxoah SA's hypoglossal stimulator for sleep apnea has an external power source, eliminating the implanted pulse generator that the stimulators on the market today include.

accepts the related long-term oral rehabilitation course and potential for lower facial sensory deficits. But multiple procedures mean additive short-term morbidity and potentially greater risk, so over time I observed patients to be less and less interested in having skeletal surgery. The quest became "less, not more surgery" for most patients. For this reason, though MMA is an excellent option for AHI and quality of life treatment,[11] few of my patients are willing to accept it.

In the last decade, a new era of pharyngeal surgery was pioneered by Michel B. Cahali, MD, who understood that modifying the lateral pharyngeal walls was key to achieving airway expansion for OSA at the upper pharyngeal bottleneck.[15] The technique involved release and resuspension of the lateral wall muscles, the palatopharyngeus, and superior constrictor. The initial version of the procedure was associated with significant dysphagia, however. Tucker Woodson, MD, subsequently modified it and devised the expansion sphincter pharyngoplasty (ESP) procedure, limiting muscle dissection to the palatopharyngeus to reduce morbidity.[16] These procedures were associated with higher AHI efficacy compared with UPPP.

I began utilizing ESP in 2007 and then, as lateral pharyngoplasty was further modified to reduce morbidity in subsequent versions, I incorporated the modifications as well, using both as my primary pharyngeal procedures. From the beginning, I incorporated Coblation dissection (saline-cooled radiofrequency dissection), as my own modification, to potentially further decrease pain. I then analyzed patients' outcomes and noted that AHI reduction could be achieved utilizing these procedures alone, even in patients who had diffuse pharyngeal collapse, including the tongue base level.[17] Thus the newer pharyngoplasty techniques eliminated the need for tongue base surgery for many of my patients. Lateral pharyngoplasty techniques are evolving further with versions such as zed-plasty, relocation pharyngoplasty,[18] and, most recently, barbed repositioning pharyngoplasty described by Mario Mantovani, MD,[19] and Claudio Vicini, MD.[20]

ROLE OF NASAL SURGERY

Nasal surgery is an important adjunctive OSA treatment. It may include the nasal valve, septum, turbinates, and nasal polyposis. Nasal breathing improves sleep quality, pulmonary reflexes, and is the most efficient route of breathing in sleep. Additionally, nasal obstruction is an impediment to OSA success; use of oronasal or full face PAP interfaces rather than nasal ones is associated with lower success rate and higher PAP pressures. Oral appliances are also thought to be poorly tolerated in those with nasal obstruction. Septal deviation can disrupt sleep if the patient sleeps with the unobstructed side dependent; it can also lead to treatment problems due to awakening from congestion. So, although nasal surgery infrequently reduces the AHI, it can play an important role in facilitating OSA treatments.

HYPOGLOSSAL NEUROSTIMULATION: A NEW FRONTIER

OSA is complex, related to small airway size, neuromuscular tone, respiratory control, and arousal threshold. Until recently, all major treatments have only targeted mechanical stabilization of the airway. Neurostimulatory approaches are now a reality—a new frontier of OSA treatment.

The tongue base was always an elusive target for treatment of the upper airway. Initially, morbid resection was performed using laser or cold steel. Then, genioglossus advancement was employed but its effect and precise application were uncertain. Tongue suspension suture techniques were also devised but appeared to have limited duration of effectiveness. Radiofrequency was then applied to stiffen the tongue base and subsequently Coblation or robot-assisted methods were used to debulk it. Finally, implantable hypoglossal neurostimulation (HGN) was introduced to activate and mold the tongue rather than resect or scar it.

In 2009, I was approached by 3 HGN companies—Apnex Medical, Inspire Medical, and ImThera Medical—to participate in their trials. I joined ImThera Medical's trial as a primary investigator. I liked its elegance as it only required a pulse generator (PG) and nerve cuff to be implanted, without a respiratory sensor.

ImThera Medical's system is investigational in the United States, presently in pivotal trial testing. It is commercially available in Europe under CE mark. Inspire Medical's device has been US FDA-approved since 2014 and has been implanted in many patients at selected US centers. Apnex Medical's device is not available as the company was shut down after disappointing trial results. Inspire's and ImThera's systems are targeted for patients with moderate to severe OSA who are intolerant of other treatments. In clinical trials, these devices have shown significant AHI reduction and improved quality of sleep and of life, though not in all patients.

From the first patient in whom I activated the implant system, I noted the pharyngeal walls lateralized and stiffened with stimulation, opening and stabilizing the upper airway. So I surmised the main effect of the hypoglossal stimulation system was via the tongue's mechanical connections with the lateral pharyngeal walls and to some degree the palate. Stimulation is carefully adjusted so to not arouse the patient from sleep. Patients turn on the system using a remote control, which activates the PG after a delay (to allow the patient to fall asleep). The PG eventually needs to be replaced, similar to a cardiac pacemaker, but replacement only requires local anesthesia (it is subcutaneous).

Like with any new therapy, there are challenges ahead. Patient acceptance of an electronic implant is not universal but will likely increase, given our growing link and dependence on technological devices and also via further device miniaturization. The initial devices were not labeled as MRI compatible, but subsequent versions can overcome this issue, also increasing acceptance. The systems' cost is high, largely attributed to the implanted PG, so insurance carriers still consider the technology "investigational" and so far approve it sporadically and only after appeals. But at the same time, the cost of untreated OSA can be quite high, thus the value analysis of implanted stimulators may be favorable. Finally, a major challenge is identifying the best patient features for optimal outcome. Inspire Medical uses sleep endoscopy to identify severe collapsibility as an exclusion. ImThera's pivotal trial criteria exclude severe hypoxemia and high apnea index, possibly also to limit extreme collapsibility. But more reliable criteria are still needed, perhaps some that will determine tongue-lateral wall mechanical coupling.

Additional experimental systems are in preliminary testing. Nyxoah SA, a company for which I serve as consultant, has developed a system with an external power source, eliminating the need and cost of an implanted pulse generator. The system is capable of bilateral stimulation of the hypoglossal branches to the genioglossus muscle. The button-like power source is applied on a patch under the chin at bedtime and removed for charging after use. The system has begun testing in European and Australian centers.

It is an exciting time to be in the field, as no doubt there will be great advances and refinements of these technologies.

WHAT ABOUT PROCEDURES FOR PRIMARY SNORING?

Finally, we must address snoring, as perhaps the most disruptive aspect of abnormal breathing in sleep. How does one help the snorer without OSA? Certainly, there are lifestyle factors that can be modified, such as smoking, alcohol, and supine positioning. Facilitating nasal breathing by treating allergies and anatomical nasal obstruction using procedures or mechanical dilators may help some. Others may benefit from mouth closure or lip suspension at night using tape or a chin strap. Expiratory positive airway pressure (EPAP) devices, such as Theravent, can also be beneficial. Many patients, however, simply wish a procedure to "fix" snoring and not depend on an ongoing treatment.

Surgical procedures for snoring have evolved and now have improved efficacy. But patient expectations should be set reasonably for snoring reduction, and some patients may need adjunctive treatments. Palatal stiffening has been performed for many years using radiofrequency, laser, chemical injection, and Pillar inserts, but often I have found these procedures to not be efficacious enough alone. I find that releasing the posterior and lateral palatal webbing (elongated palatal curtain) under local anesthesia is key to decrease snoring. Over the last few years, for some patients, I have also added barbed suture suspension. Barbed sutures have micro-grips that allow me to obtain a palatal lift. The combination of stiffening, shortening the vibratory segment, and lifting can produce excellent results for many pat ients. **SR**

Ofer Jacobowitz, MD, PhD, FAASM, called "Dr J" by his patients, is a fellow of the AASM, board certified sleep specialist and otolaryngologist, and head and neck surgeon. He is past chair of the AASM's Sleep-related Breathing Disorders section and of all membership sections. He is an assistant professor at Mount Sinai Hospital in NY. Visit his practice's website at www.entandallergy.com/jacobowitz.

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